



Prithwiraj Maiti

A Practical Handbook of **PATHOLOGY** Specimens and Slides



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Prithwiraj Maiti

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Dedicated to

All my juniors

Preface

The 2nd Professional MBBS examination is tough as it comes with a very wide syllabus, which a yet-newcomer medical student has to cover in a short time. For the pathology part, the systemic pathology remains an area of fear for many students as it looks lengthy and actually it is. The idea of this book came from this point.

It is a common fact everywhere that the questions asked in the Pathology Grand Viva actually start from the specimens and many students, even after reading their textbooks for 3 to 4 times remain very afraid of what questions will actually be asked. This book has covered a huge portion of systemic pathology and I think it will be helpful both for your theory as well as viva examinations. This book is not a textbook, but a supplement to textbooks.

As I am only in my Final Year MBBS and have a lot of things still unknown to me, I request everyone for any kind of feedback about this book. Please email me at prithwiraj2009@yahoo.in for any suggestions, queries or recommendations. I think this book will be a true companion of you at examination times. Thank you.

Prithwiraj Maiti

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At the very beginning, I want to thank my parents, who have loved me always and have inspired me every moment to do something new. For the most of the photographs are taken by my friends Suvadeep Mandal and Debojyoti Dutta, the picture courtesy goes to them. I also want to thank my friends Suman Mandal and Bhaskar Roychoudhury for always staying with me and giving continuous support. My heartfelt thanks goes to all the staff of Jaypee Brothers Medical Publishers (P) Ltd family for working days and night to make this book a beautiful one especially to Shri Jitendar P Vij (Group Chairman), Mr Ankit Vij (Group President) and Mr Tarun Duneja (Director–Publishing) of M/s Jaypee Brothers Medical Publishers (P) Ltd, New Delhi, India, for publishing this book. I especially want to thank Mr Sabyasachi Hazra for his efforts towards publishing this 1st edition. At the end, the support from all my juniors is worth mentioning, because without their suggestions and feedbacks, it would be impossible to improvise the contents of this book. They have done the tough job of criticizing, which was also a main reason of student-friendliness of this book. Last but not least, it is worthy to mention those renowned pathologists and doctors who have accepted contributing their beautiful photographs in this book.

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Contents

| SECTION — I | SPECIMENS | 1–98 |
|--|---|--------------|
| Chapter 1: Cardiovascular System | | 3–19 |
| | <ul style="list-style-type: none">• Mitral stenosis 3• Subacute bacterial endocarditis (SABE) 9• Atheroma 11• Left ventricular hypertrophy 14• Fibrinous pericarditis 17 | |
| Chapter 2: Gastrointestinal Tract | | 20–33 |
| | <ul style="list-style-type: none">• Stomach 20<ul style="list-style-type: none">– Peptic ulcer 20– Gastric carcinoma 23• Small intestine 27<ul style="list-style-type: none">– Tuberculous ulcer 27– Typhoid ulcer 29• Large intestine 31<ul style="list-style-type: none">– Colon carcinoma 31 | |
| Chapter 3: Liver | | 34–48 |
| | <ul style="list-style-type: none">• Basic histological anatomy of liver 34• Fatty liver 35• Cirrhosis of liver 40• Metastatic carcinoma of liver 47 | |
| Chapter 4: Kidney | | 49–62 |
| | <ul style="list-style-type: none">• Large white kidney 49• Granular contracted kidney 52• Hydronephrosis 55• Polycystic kidney disease 57• Renal cell carcinoma 60 | |
| Chapter 5: Male Genital System | | 63–67 |
| | <ul style="list-style-type: none">• Carcinoma penis 63• Seminoma testis 64• Benign hypertrophy of prostate/benign prostatic hyperplasia 65 | |
| Chapter 6: Female Genital System | | 68–73 |
| | <ul style="list-style-type: none">• Leiomyoma of uterus 68• Carcinoma cervix 69• Dermoid cyst/benign cystic teratoma 72 | |

Chapter 7: Breast **74–77**

- Breast carcinoma 74

Chapter 8: Bones and Joints **78–86**

- Sequestrum 78
- Tuberculosis of spine (Pott's disease) 81
- Giant cell tumor of bone 82
- Osteosarcoma 84

Chapter 9: Respiratory System **87–98**

- Lobar pneumonia of lung 87
- Miliary tuberculosis of lung 90
- Fibrocaseous tuberculosis of lung 90
- Tuberculosis 91
- Bronchogenic carcinoma 94
- Bronchiectasis 97

SECTION — II **SLIDES** **99–110**

Chapter 10: Pathology Practical Slides Identification **101–110**

- Acute appendicitis 101
- Chronic cholecystitis 101
- Colloid goiter 102
- Capillary hemangioma 102
- Cavernous hemangioma 102
- Tuberculosis of lymph node 103
- Tuberculosis of intestine 103
- Adenocarcinoma 103
- Secretory endometrium 104
- Proliferative endometrium 104
- Benign hypertrophy of prostate (BHP) 104
- Lipoma 105
- Cirrhosis of liver 105
- Fatty liver 105
- Mucinous cystadenoma of ovary 106
- Basal cell carcinoma of skin 106
- Squamous papilloma of skin 106
- Squamous cell carcinoma of skin 107
- Malignant melanoma of skin 107
- Scirrhus carcinoma of breast 108
- Fibroadenoma of breast 108
- Renal cell carcinoma 108
- Pleomorphic salivary adenoma 109
- Seminoma testes 109
- Giant cell tumor of bone 109

- Osteosarcoma 110
- Chronic lymphocytic leukemia (CLL) 110
- Chronic myeloid leukemia (CML) 110

Bibliography 111

Index 113

SECTION-I

SPECIMENS

Cardiovascular System

CHAPTER

1

Mitral stenosis

Description

- It is a specimen of heart cut transversely.
- The left ventricle is recognized by its thick wall.
- The valve is lying between left ventricle and left atrium and having 2 cusps. So it is **mitral valve**.
- The valve has become thickened and fibrosed.
- The orifices have become grossly narrowed.
 - So, the specimen is identified as “Mitral stenosis” (Fig. 1.1).

What do you mean by stenosis?

Stenosis is the failure of a valve to open completely, which impedes forward flow (Fig. 1.2).

What do you mean by regurgitation/insufficiency?

Regurgitation is the failure of a valve to close completely, thereby allowing reversed flow.

What is the major cause of mitral stenosis?

The major cause of mitral stenosis in India is chronic rheumatic heart disease.

Which age group is mostly affected?

School children (5–15 years age group).

What is the causative agent of rheumatic fever (RF) and rheumatic heart disease (RHD)?

- RF is a delayed autoimmune response to Group A streptococcal pharyngitis.

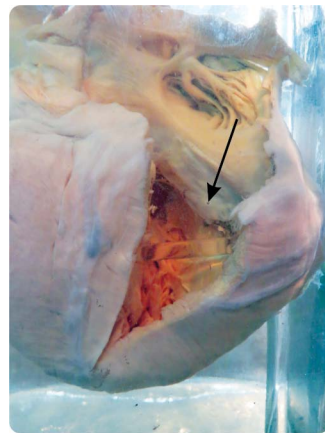


Fig. 1.1: Mitral stenosis. Specimen of heart, cut open to show cusps of mitral valve, which are thickened (arrow) and the opening is narrowed



Fig. 1.2: Autopsy specimen showing thickened mitral valve leaflets with marked stenosis. Reproduced under the permission of Dr Jeremy Jones and Radiopaedia.org

- The clinical manifestations and severity of the disease depends on:
 1. Genetic susceptibility of the host
 2. Virulence of the infecting organism
 3. A favorable environment.
- Although streptococci from serogroups B, C, G, and F can cause pharyngitis, they are not linked to the etiology of RF or RHD.

Describe the pathogenesis of RF/ RHD.

- *Acute rheumatic fever (ARF) results from delayed immune responses to group A streptococcal antigens.*
- *Antibodies directed against the M-proteins of streptococci have been shown to cross-react with self-antigens in the heart.*
- *In addition, CD4+ T cells specific for streptococcal peptides react with self-proteins of the heart and produce cytokines that activate macrophages and damage heart tissue.*
- *So, the damage to the heart tissue is thought to be caused by a combination of antibody and T cell-mediated reactions.*
- *The actual sequential events in the pathogenesis of RF/RHD is shown in Figure 1.3.*

Note: Acute rheumatic fever never causes mitral stenosis in its first episode; but it may occur during recurrence and reactivation of the organism.

What is the role of streptococcal “M-protein” in the pathogenesis of RHD?

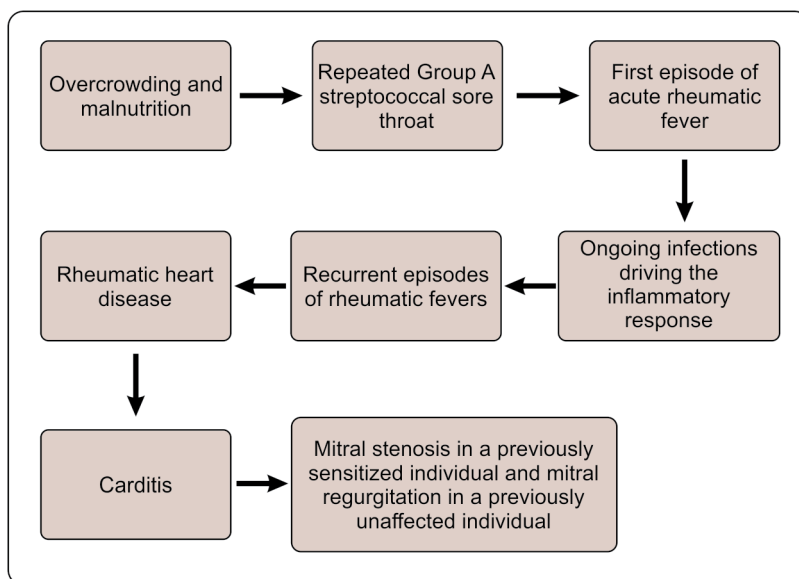
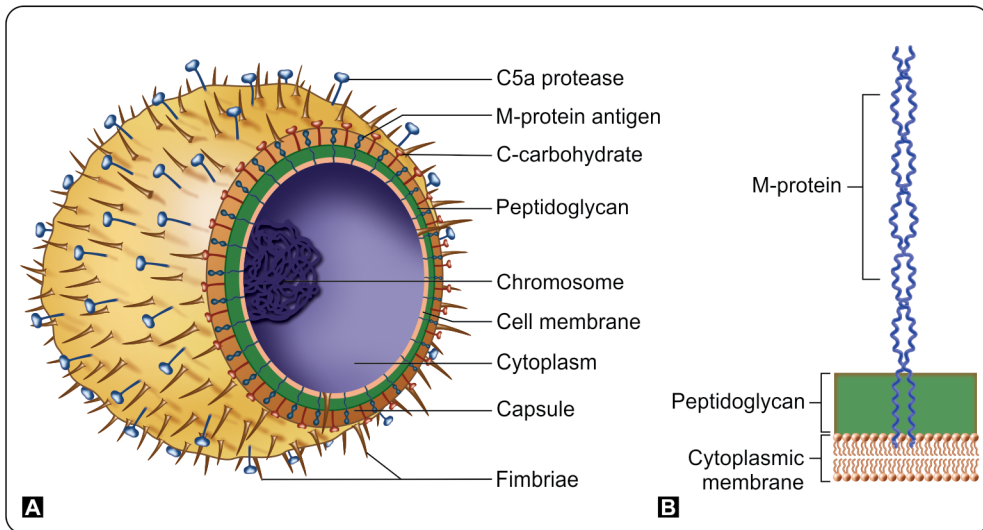


Fig. 1.3: Pathogenesis of mitral stenosis in RF/RHD



Figs 1.4A and B: A. Structure of a streptococcal cell, B. M-protein and its extension

- M-protein is one of the best-defined determinants of bacterial virulence in RHD.
- *The streptococcal M-protein extends from the surface of the cell as an alpha-helical coiled dimer (Figs 1.4A and B), and shares structural homology with cardiac proteins (myosin, tropomyosin and laminin); which are integral part of the cardiac valve and myocardium.*
 - It has been suggested that this homology is responsible for the characteristic pathological findings in acute rheumatic carditis.

What is the “toxic immunological hypothesis” of RF and RHD?

This hypothesis states that *some components of Group A streptococci have antigenic cross-relationship with human tissues* which is mostly responsible

for their reaction against self-tissue antigens and also for the characteristic clinical manifestations found in RF/ RHD.

What are the cardinal anatomic changes in the mitral valve?

1. Leaflet thickening
2. Commissural fusion and shortening
3. Thickening and fusion of tendinous cords.

| Bacterial components | Cross antigenic reaction against which host tissue? |
|-------------------------|---|
| Capsule hyaluronic acid | Human synovial fluid and myocardium |
| Group A carbohydrate | Heart valve |
| M protein | Heart valve and myocardium |
| Cytoplasmic membrane | Vascular lamina |
| Peptidoglycan | Skin |

What will be the microscopic appearance of the mitral valve?

Microscopically, the changes found in the mitral leaflets are:

1. Acute inflammation
2. Diffuse fibrosis
3. Neovascularization (new blood vessels formation).
 - This will eventually obliterate and destroy the leaflet architecture.

Questions about 'Aschoff body'

What is an 'Aschoff body'?

Aschoff bodies are pathognomonic lesions of rheumatic heart disease, characterized by presence of nodules in the heart

resulting from inflammation of the heart tissue (Fig. 1.5).

Where they are predominantly found?

Usually in the myocardium and endocardium, in the vicinity of small blood vessels.

What is their microscopic appearance?

Microscopically, Aschoff body contains the following:

1. Anitschkow/Caterpillar cells: Activated macrophages characterized by linear condensations of nuclear chromatin (Fig. 1.6).
2. Foci of T-lymphocytes.
3. Necrosed collagen fibers.

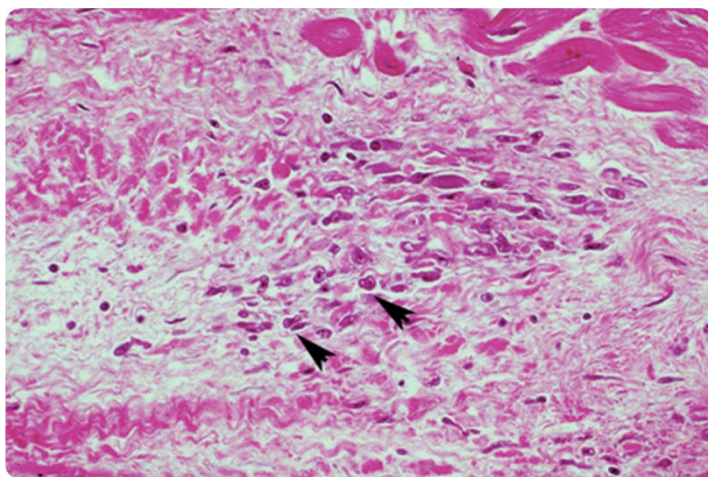


Fig. 1.5: Aschoff bodies (arrow heads): An interstitial aggregate of macrophages and lymphocytes with areas of fibrosis. Image reprinted with permission from Allen Patrick Burke, MD, University of Maryland School of Medicine, published by Medscape Reference (emedicine.medscape.com; 2013, available at: emedicine.medscape.com/article/1962779-overview)

What are the stages of evolution of Aschoff bodies?

| <i>Time of illness</i> | <i>Name of the stage</i> | <i>Characteristic features of the stage</i> |
|------------------------|--------------------------|--|
| 4th week | Early exudative stage | <ul style="list-style-type: none"> • Edema of connective tissue • Increase in ground substance • Separation and eventual fragmentation of collagen fibers |

Contd...

Contd...

| Time of illness | Name of the stage | Characteristic features of the stage |
|-----------------|----------------------------------|--|
| 4th–13th week | Intermediate proliferative stage | <ul style="list-style-type: none"> Staining of the area characteristic of fibrin (fibrinoid necrosis) <p>This is the stage of Aschoff bodies, characterized by presence of:</p> <ul style="list-style-type: none"> Anitschkow cells Foci of T-lymphocytes Necrosed collagen fibers |
| 12th–16th week | Late fibrotic stage | <ul style="list-style-type: none"> Fibrosis of Aschoff bodies occurs Eventually, cellularity of Aschoff body decreases and it is replaced by a small fibrocollagenous scar |

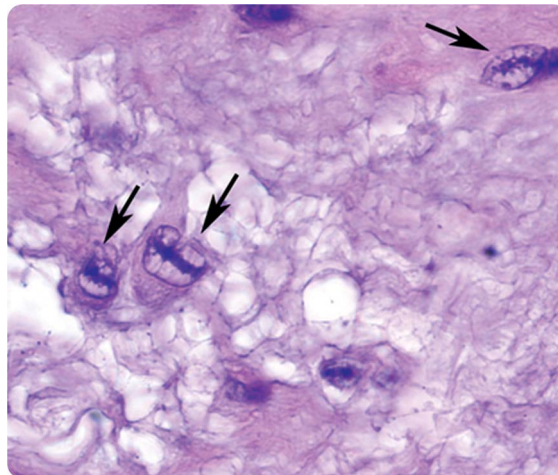


Fig. 1.6: Anitschkow cells/Caterpillar cells (arrows): Present in the center of Aschoff bodies and identified by the presence of linear condensation of nuclear chromatin. Image reprinted with permission from Allen Patrick Burke, MD, University of Maryland School of Medicine, published by Medscape Reference (emedicine.medscape.com; 2013, available at: emedicine.medscape.com/article/1962779-overview)

Which ventricle will be affected more?

- Long-standing congestive changes in the lungs induce pulmonary vascular and parenchymal changes, eventually leading to *right ventricular hypertrophy*.
- The left ventricle is largely unaffected by an isolated mitral stenosis.

Which are the clinical findings of cardiac involvement in RHD?

| Inflammation of cardiac layers | Clinical findings |
|--------------------------------|---|
| Pericarditis | Audible friction rub |
| Myocarditis | Unexplained CHF/ cardiomegaly; almost always associated with valvular involvement |
| Endocarditis/valvulitis | Presence of murmur of mitral regurgitation |

Which is the most common ECG change found in RHD?

First degree AV block.

How will you diagnose RF and RHD?

2002–2003 WHO criteria for the diagnosis of rheumatic fever and rheumatic heart disease (based on the revised Jones criteria):

| <i>Diagnostic categories</i> | <i>Criteria</i> |
|--|---|
| Primary episode of RF ^a | Two major * or one major and two minor **manifestation plus evidence of a preceding Group A streptococcal infection*** |
| Recurrent attacks of RF in a patient without established rheumatic heart disease ^b | Two major or one major and two minor manifestation plus evidence of a preceding Group A streptococcal infection |
| Recurrent attacks of RF in a patient with established rheumatic heart disease | Two minor manifestation plus evidence of a preceding Group A streptococcal infection ^c |
| Rheumatic chorea Insidious onset rheumatic carditis | Other major manifestations of evidence of Group A streptococcal infection not required |
| Chronic valve lesions of RHD (patients presenting for the first time with pure mitral stenosis or mixed mitral valve disease and/or aortic valve disease) ^d | Do not require any other criteria to be diagnosed as having rheumatic heart disease |
| * Major manifestations | <ul style="list-style-type: none"> — Carditis — Polyarthritis — Chorea — Erythema marginatum — Subcutaneous nodules |
| ** Minor manifestations | <ul style="list-style-type: none"> — Clinical: Fever, polyarthralgia — Laboratory: Elevated acute phase reactants (erythrocyte sedimentation rate or leukocyte count) |
| *** Supporting evidence of a preceding streptococcal infection within the last 45 days | <ul style="list-style-type: none"> — Electrocardiogram: Prolonged P-R interval — Elevated or rising antistreptolysin-O or other streptococcal antibody, or — A positive throat culture, or — Rapid antigen test for Group A streptococcus, or — Recent scarlet fever |
| ^a Patients may present with polyarthritis (or with only polyarthralgia or monoarthritis) and with several (3 or more) other minor manifestation, together with evidence of recent Group A streptococcal infection. Some of these cases may later turnout to be rheumatic fever. It is prudent to consider them as cases of 'probable rheumatic fever' (once other diagnoses are excluded and advise regular secondary prophylaxis. Such patients require close follow-up and regular examination of the heart. This cautious approach is particularly suitable for patients in vulnerable age groups. | |
| ^b Infective endocarditis should be excluded. | |
| ^c Some patients with recurrent attacks may not fulfill these criteria. | |
| ^d Congenital heart disease should be excluded. | |

What are the effects of mitral stenosis on different organs?

| Organs | Effects |
|-------------------|---|
| Heart | |
| Left ventricle: | Normal |
| Right ventricle | |
| Left atrium | Dilation and hypertrophy |
| Right atrium | |
| Lungs | The lungs are heavy, voluminous, firm and brownish in color |
| Liver | Nutmeg liver (cut surface shows alternate dark and pale area, major cause is congestive cardiac failure) |
| Spleen | Congestive splenomegaly |
| Kidney | Congestion and proteinuria |
| Peritoneum | Ascites |

What are the complications of mitral stenosis?

1. Recurrent hemoptysis
2. Congestive cardiac failure
3. Atrial fibrillation
4. Embolism
5. Dysphagia
6. Subacute bacterial endocarditis (Fig. 1.7).

Subacute bacterial endocarditis (SABE)

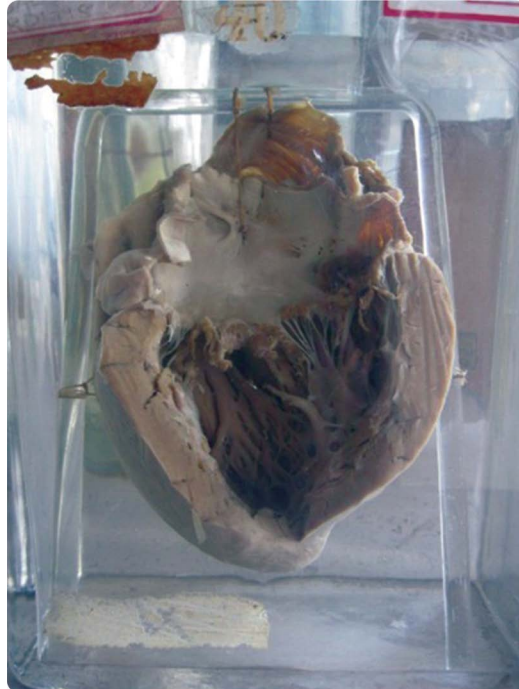


Fig. 1.7: Subacute bacterial endocarditis (SABE)

Description

This is a specimen of heart showing evidence of damage to valve cusps and having vegetations which are brownish in color.

- So the specimen is identified as “Subacute bacterial endocarditis” (Fig. 1.7).

What are the causative bacteria?

Subacute bacterial endocarditis is usually caused by low virulence organism. For example:

1. *Strep. viridans* (most common)
2. *Strep. faecalis*
3. HACEK group of bacteria (*Haemophilus*, *Actinobacillus*, *Cardiobacterium*, *Eikenella*, and *Kingella*).

What is the most common site of vegetation?

Damaged mitral valve after a previous episode of rheumatic heart disease (RHD) (Fig. 1.8).



Fig. 1.8: Mitral valve: Endocarditis with large vegetation on the atrial aspect of the valve. The underlying chordae are relatively unremarkable. Image reprinted with permission from Allen Patrick Burke, MD, University of Maryland School of Medicine, published by Medscape Reference (emedicine.medscape.com; 2013, available at: emedicine.medscape.com/article/1954887-overview)

What are the known conditions that expose the heart to an episode of SABE?

1. A previously damaged heart
2. Previous episode(s) of bacteremia.

What are the risk factors for SABE?

1. Mitral valve prolapse
2. Degenerative calcific valvular stenosis
3. Bicuspid aortic valve
4. Artificial (prosthetic) valves.

Describe the pathogenesis of SABE.

- Transient low virulence bacteremia has minimal ill effects on a normal endocardium.
- But when the bacteria get implanted on a previously damaged valve/mural endocardium, they produce vegetations.
- SABE is thought to be a *type 3 hypersensitivity reaction* (i.e. antigen antibody complexes; when not cleared adequately by immune cells, gives rise to an inflammatory reaction).

What is the typical microscopic picture of a SABE?

- Microscopically, the vegetations of a

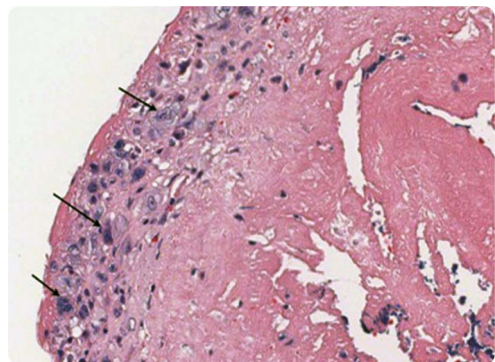


Fig. 1.9: Infective endocarditis, surface of valve leaflet with fibrin and macrophages (arrows), which are seen in the acute and subacute phases of inflammation. Image reprinted with permission from Allen Patrick Burke, MD, University of Maryland School of Medicine, published by Medscape Reference. (emedicine.medscape.com; 2013, available at: emedicine.medscape.com/article/1954887-overview)

typical SABE have granulation tissue indicative of healing at their bases.

- With time, fibrosis, calcification and a chronic inflammatory infiltrate (presence of macrophages) can develop (Fig. 1.9).

What are the complications of SABE?

| Site | Complications |
|--------------|--|
| Cardiac | <ul style="list-style-type: none"> • Focal degenerative changes • Necrosis of the myocardium • Rupture of the interventricular septum |
| Extracardiac | <ul style="list-style-type: none"> • Microthromboemboli formation • Retinal hemorrhages (Roth spots) • Painful subcutaneous nodules on the pulp of the digits (Osler's node) • Painless erythematous lesions of palm/sole (Janeway lesions) • Hematuria due to immune complex • Glomerulonephritis |

between SABE and acute bacterial endocarditis?

| Acute bacterial endocarditis | Subacute bacterial endocarditis |
|---|---|
| It is caused by highly virulent organism (e.g. <i>Staph. aureus</i>) | It is caused by organism of low virulence (e.g. <i>Strep. viridans</i>) |
| It affects the normal heart | It affects only the previously damaged heart valve/mural endocardium |
| It is associated with multiple pyogenic abscess formation as the emboli contains virulent organism | Here usually no/single abscess is seen |
| The microscopic picture is of an acute inflammation as the valve cusps show congestion/necrosis/ulceration/perforation | The microscopic picture is of a chronic inflammation as the vegetations show granulation tissue/fibrosis/calcification/a chronic inflammatory infiltrate |

What are the differentiating points

Atheroma



Figs 1.10A and B: Atheroma

Description

- Specimen showing a large artery cut open to expose intimal surface (identified by ostia of branch vessels).
- The intima is showing **raised pearly white plaque** close to the opening of ostia of branch vessels.
 - So, the specimen is identified as **“Atheroma of a large blood vessel”** (Figs 1.10A and B).

What are the arteries commonly affected?

1. Abdominal aorta
2. Coronary arteries
3. Cerebral arteries.

Name some of the common risk factors for atheroma formation.

1. Hyperlipidemia
2. Hypertension
3. Diabetes mellitus
4. Cigaret smoking.

Mention the main steps of “Response to injury” hypothesis of atherosclerosis.

According to this hypothesis, atherosclerosis is a chronic inflammatory response and also an attempt of healing of the arterial wall to endothelial injury. The steps are as follows: (Figs 1.11 and 1.12)

Name the different stages in the evolution of atheroma.

1. Fatty streaks
2. Atherosclerotic plaque
3. Complicated atherosclerotic plaques.

Describe the different stages in the evolution of atheroma.

Fatty streaks:

- Fatty streaks are the earliest lesions in the evolution of atherosclerosis.
- They are composed of LDL-filled foamy macrophages (or foam cells) located beneath the endothelium of an artery.
- At first, they are visualized as multiple minute flat yellow spots, but eventually they coalesce to form elongated streaks.
- These lesions do not cause any flow disturbance and are clinically silent.

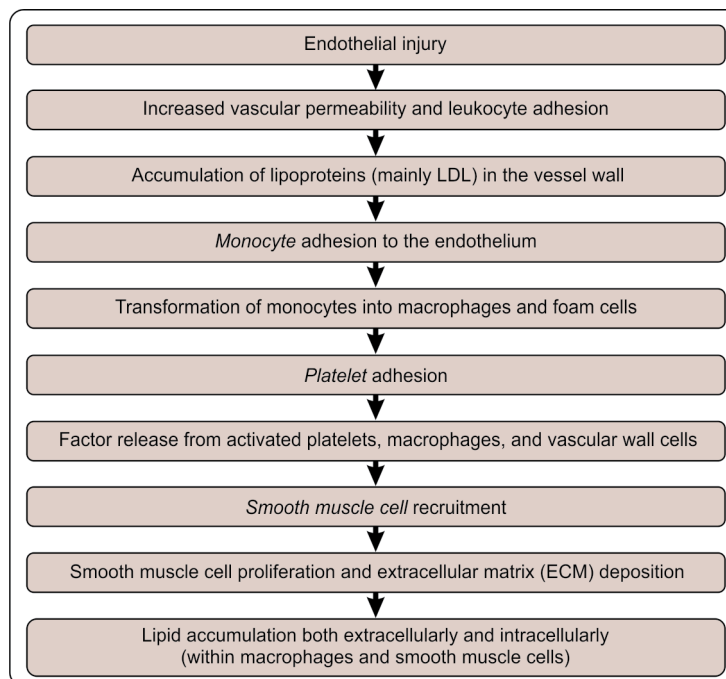


Fig. 1.11: Pathogenesis of atherosclerosis (steps)

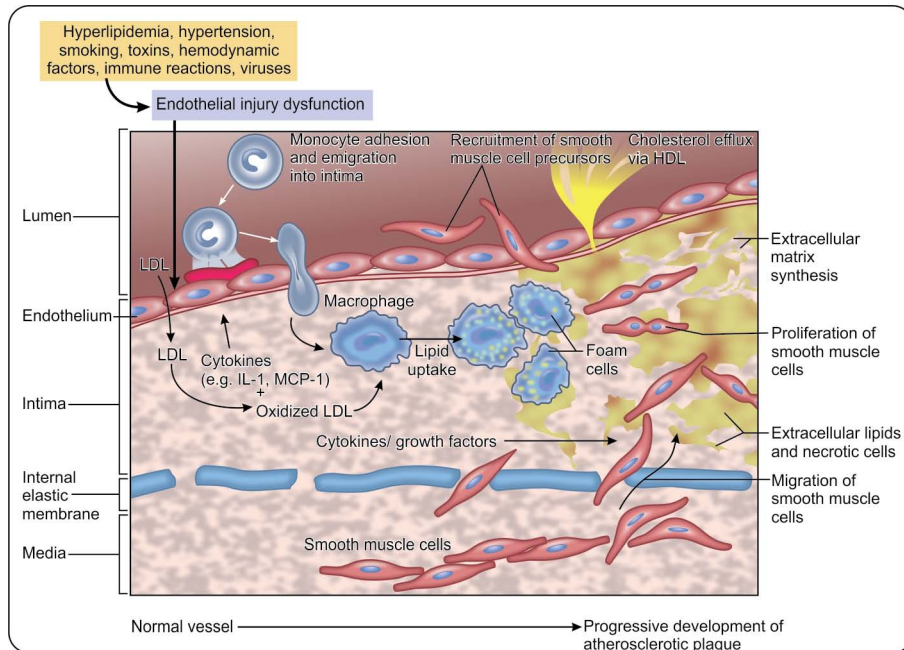


Fig. 1.12: Pathogenesis of atherosclerosis (graphical representation)

Atherosclerotic plaque:

- They are white to yellow plaques on the lumen of the artery; about 0.3–1.5 cm in diameter, resulting from lipid accumulation and intimal thickening.
- A typical atherosclerotic plaque consists of the following components (Fig. 1.13).

| Components | Contents |
|--------------------------------|--|
| A necrotic core at the center | <ul style="list-style-type: none"> • Cell debris • Cholesterol • Cholesterol esters • Foam cells |
| A fibrous cap in the periphery | <ul style="list-style-type: none"> • Collagen and elastin • Smooth muscle cells • Foam cells • Macrophages • Lymphocytes • New blood vessels |

Complicated atherosclerotic plaque:

A mature atherosclerotic plaque is susceptible to the following complications:

1. Ulceration of the plaque.

2. Rupture of the plaque (an unstable plaque ruptures easily).
3. Thrombosis (due to plaque rupture and release of highly procoagulant substances*into the bloodstream).
4. Emboli formation (due to plaque rupture).
5. Hemorrhage into the plaque (due to presence of weak new vessels in the fibrous cap).
6. Aneurysm formation (due to ischemia of the media of the blood vessels and resulting weakness of the vessel wall).

The major consequences of a complicated atherosclerotic plaque are:

| Involved organs | Consequence |
|-----------------|-----------------------|
| Heart | Myocardial infarction |
| Brain | Cerebral infarction |
| Lower extremity | Gangrene of the legs |
| Great vessels | Aneurysm of the aorta |

(*Example: Tissue factor and plasminogen activator Inhibitor (PAI) from endothelial cells and release of active granules from platelets)

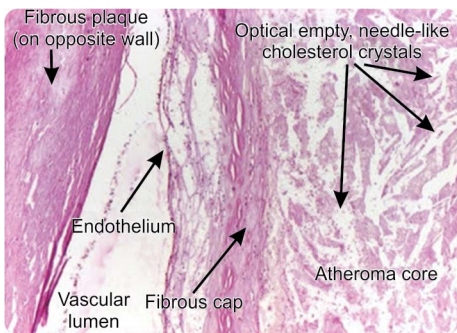


Fig. 1.13: Structure of an atherosclerotic plaque: Reproduced under the permission of Dr Mihai Danciu, Gr T Popa University of Medicine and Pharmacy, Iasi, Romania

What do you mean by a stable and an unstable plaque?

The atheromatous plaques may have two types of progression (Fig. 1.14):

Stable plaques:

- The atheromatous plaques may grow slowly due to gradual accumulation of lipids in the foam cells.
- The fibrous cap in these plaques gets

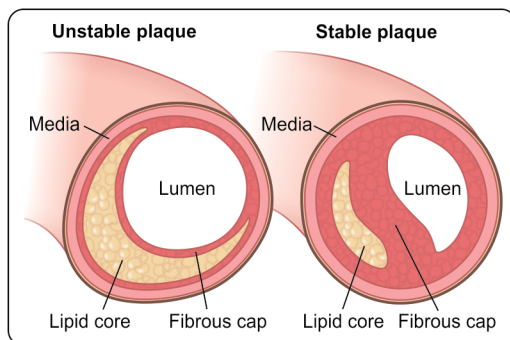


Fig. 1.14: Structure of a stable plaque and an unstable plaque vulnerable to complications like rupture, ulceration and hemorrhage

matured and thickened, so they are not susceptible to rupture.

- So they are called “Stable” plaques.

Unstable plaques:

- The atheromatous plaques may grow rapidly due to rapid accumulation of lipids in the foam cells.

- The fibrous cap in these plaques is thin and prone to early rupture.
- So they are called “Unstable” plaques.

It should be remembered that once an atheromatous plaque gets ruptured, it rapidly activates platelets and the clotting cascades, rapidly resulting in an acute thrombotic event.

How does an atheroma narrow the blood vessels?

1. By presence of raised plaque
2. Thrombosis of the ulcerated plaque
3. Hemorrhage under the plaque pushing it up
4. Rupture of the plaque.

Left ventricular hypertrophy

Description

- This is a specimen of heart showing a transverse cut section of the left ventricle, which is highly thickened.
- The tendinous cords are also showing extensive thickening.
- The size of the left ventricle is increased.
- There is massive dilation of the left ventricle.
- So, the specimen is identified as “Left ventricular hypertrophy” (Fig. 1.15).



Fig. 1.15: Left ventricular hypertrophy

What is the main cause of left ventricular hypertrophy?

Left-sided heart failure, which is most often caused by:

1. Ischemic heart disease

2. Hypertension

3. Aortic and mitral valvular diseases.

What are the pathogenesis and consequences of cardiac hypertrophy?

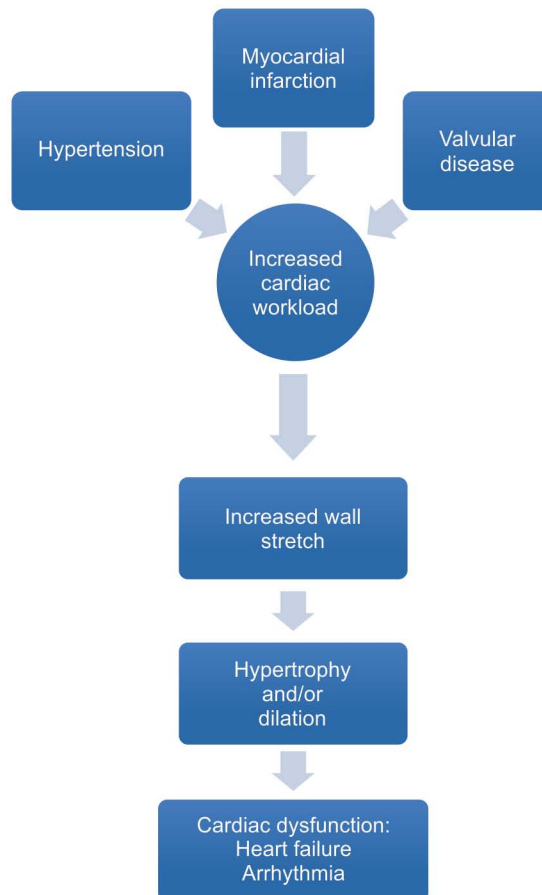


Fig. 1.16: Pathogenesis and consequences of cardiac hypertrophy

What are the changes seen in the lungs in a case of LVH?

1. Heavy and wet lungs:

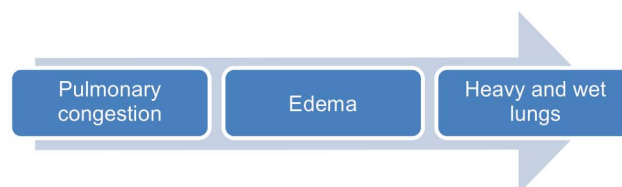


Fig. 1.17: Pulmonary congestion is characteristic of left-sided heart failure

2. Formation of "Heart failure cells":

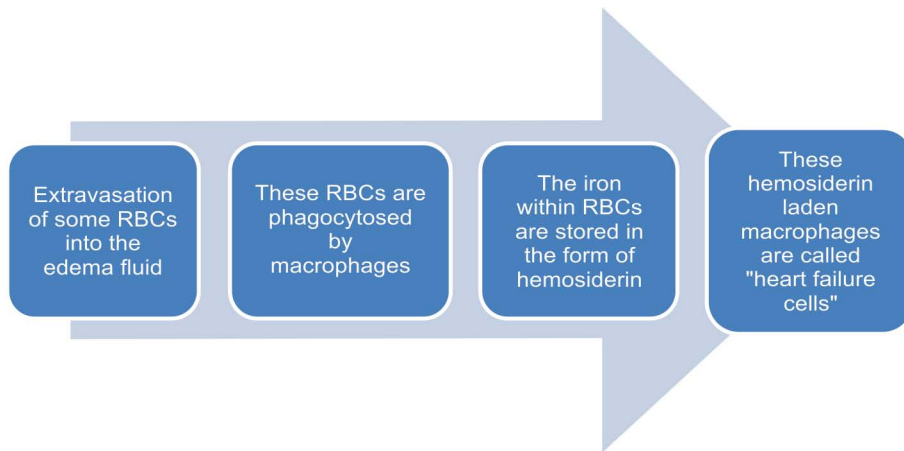


Fig. 1.18: Heart failure cells

3. The other definite changes are:



Fig. 1.19: Sequential events leading to pulmonary edema in left-sided heart failure

What are Kerley B lines?

They are 1–2 cm thin pulmonary opacities seen perpendicular to the pleural surface, representing thickened subpleural interlobular septa (Fig. 1.20).

Common causes:

1. Congestive cardiac failure
2. Pulmonary fibrosis
3. Recurrent pulmonary edema.

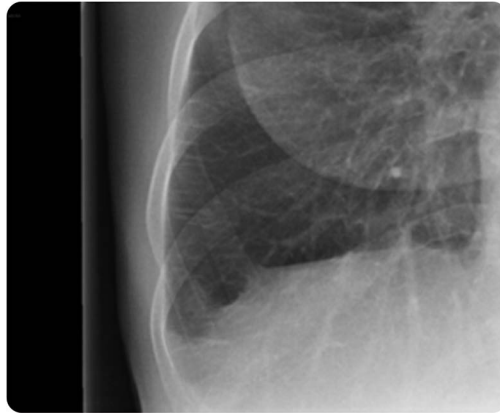


Fig. 1.20: Kerley B lines: Reproduced under the permission of Dr Sajoscha Sorrentino and Radiopaedia.org

What are the changes seen in other organs?

| Organs | Changes |
|--------|---|
| Kidney | Prerenal azotemia (because of the hypoperfusion of kidney, excretion of nitrogenous products increases significantly) |
| Brain | Hypoxic encephalopathy (due to cerebral hypoxia) |

Fibrinous pericarditis

Description

- It is a specimen of heart showing the pericardium at its outer surface.

- The surface is dry.
- The surface is also showing a **fine granular roughening**.
 - So, the specimen is identified as “Fibrinous pericarditis” (Figs 1.21A and B).



Figs 1.21A and B: Fibrinous pericarditis

What are the common causes of fibrinous pericarditis?

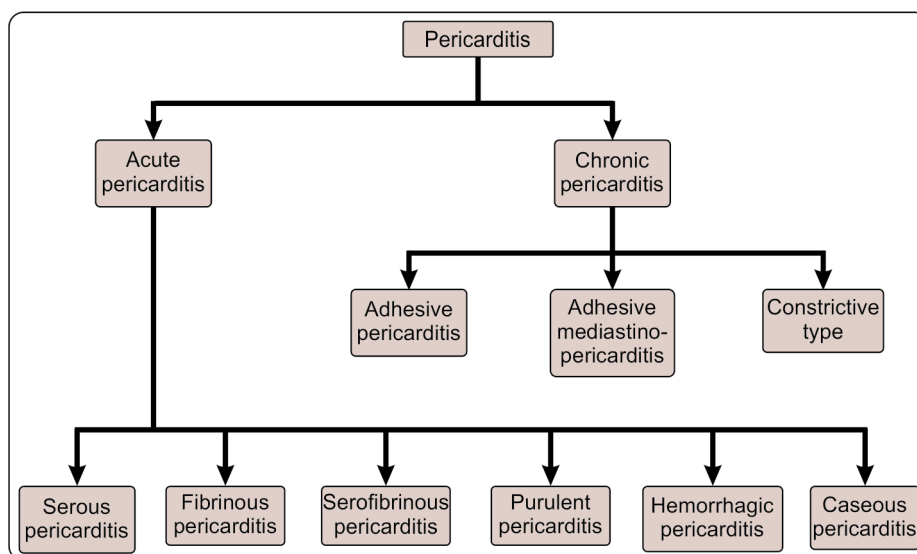
1. AMI
2. Postinfarction syndrome
3. Uremia
4. Chest radiation
5. Rheumatic fever

6. SLE

7. Trauma.

What is the most striking clinical sign of fibrinous pericarditis?

A loud pericardial friction rub.

How will you classify pericarditis?**Fig. 1.22:** Classification of pericarditis**Describe the differentiating features of different types of pericarditis.****Acute pericarditis**

| <i>Types</i> | <i>Etiology</i> | <i>Differentiating features</i> |
|----------------------------|---|---|
| Serous pericarditis | Characteristically of a sterile origin (SLE, rheumatic fever, tumors, uremia, viral infection, etc.) | Scant epicardial/pericardial mild inflammatory infiltrate |
| Fibrinous pericarditis | Most common type of pericarditis causes are described previously | Dry surface with a fine granular roughening |
| Serofibrinous pericarditis | Acute viral infection | Presence of large amount of yellow/ brown turbid exudate (filled with RBC, WBC, and fibrin) |
| Purulent pericarditis | Direct extension from adjacent infection sites (pneumonia/empyema/lung abscess, etc.). Most common agents are staphylococci, streptococci and pneumococci | Erythematous granular surface with extensive purulent exudate |

Contd...

Contd...

| <i>Types</i> | <i>Etiology</i> | <i>Differentiating features</i> |
|--------------------------|---|--|
| Hemorrhagic pericarditis | Most commonly seen after cardiac surgery; also associated with TB/ malignancy | Exudate is predominantly composed of blood admixed with fibrinous/purulent exudate |
| Caseous pericarditis | Caused by direct extension of tubercle bacilli from lymph nodes | Eventually leads to fibrocalcific constrictive pericarditis |

Chronic pericarditis

| <i>Types</i> | <i>Etiology</i> | <i>Differentiating features</i> |
|----------------------------------|--|--|
| Adhesive pericarditis | Mostly seen in rheumatic heart disease (RHD) | Adhesion between parietal and visceral pericardium that does not impair cardiac function significantly |
| Adhesive mediastino-pericarditis | Seen after an episode of purulent pericarditis/cardiac surgery/ irradiation to the mediastinum | Adhesion between 2 layers of pericardium as well as between parietal pericardium and adjacent mediastinal structures; compelling the heart to contract against all the adhesive structures; eventually leading to hypertrophy and dilation |
| Constrictive pericarditis | Tuberculosis is the most common cause | There is marked thickening and scarring of parietal pericardium, causing the heart to lose its capacity to increase cardiac output in response to increased demand in the peripheral circulation |

CHAPTER

2

Gastrointestinal Tract

Stomach

Before going into detail of description about the stomach specimens, we are briefly recapitulating the various parts of

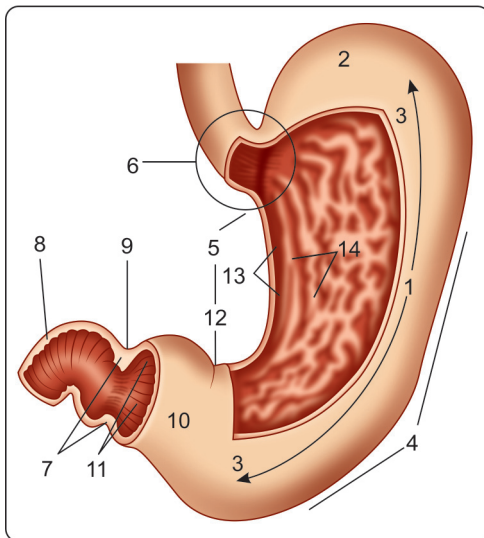


Fig. 2.1: 1. Body of stomach, 2. Fundus, 3. Anterior wall
4. Greater curvature, 5. Lesser curvature, 6. Cardia
7. Pyloric sphincter (valve), 8. Duodenum,
9. Pylorus, 10. Pyloric antrum, 11. Pyloric canal,
12. Angular notch, 13. Gastric canal, 14. Rugal folds

stomach, as it will help you to understand the site of involvement of diseases (Fig. 2.1).

Peptic ulcer

Description

This is a specimen cut open along the greater curvature of stomach, showing mucosal ulcer with the following features:



Fig. 2.2: Peptic ulcer

| Features | Description |
|----------|---|
| Location | Close to lesser curvature (95%) |
| Number | Usually single |
| Size | <2 cm in diameter |
| Shape | Oval/round |
| Margin | Sharply delineated |
| Edge | Thickened |
| Floor | Formed by serous/subserous layer and contains no muscle |

- So, the above specimen is identified as “Peptic ulcer” (Fig. 2.2).

Why this is not a specimen of gastric carcinoma?

This is not a specimen of gastric carcinoma because in the ulcerative type of gastric carcinoma the following features are found:

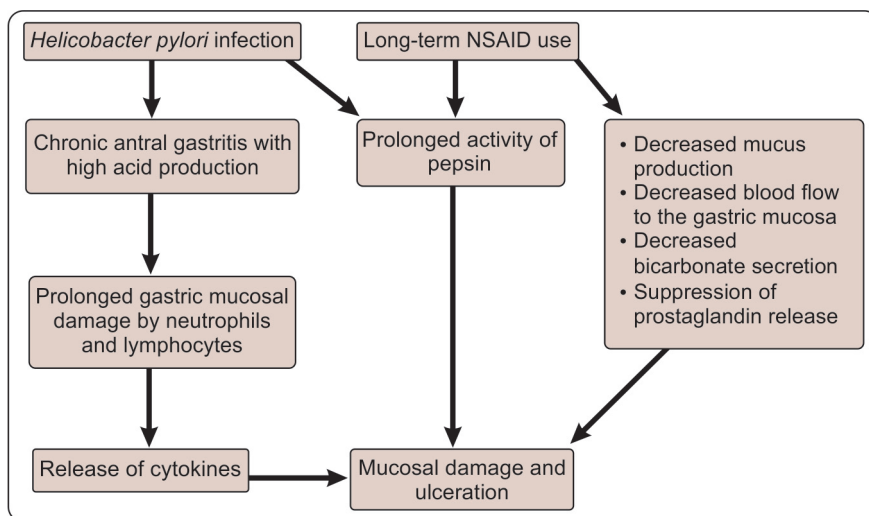
| Features | Description |
|----------|---------------------------------|
| Location | Greater curvature (most common) |
| Size | Usually >3 cm in diameter |
| Margin | Usually irregular |
| Edge | Thickened and everted |
| Floor | Formed by muscle layer |

What are the sites where gastric ulcer may be found?

1. 1st part of duodenum (most common)
2. Stomach
3. Lower part of esophagus
4. Jejunum (after gastrojejunostomy)
5. Meckel's diverticulum (with gastric type of mucosa).

Describe the pathogenesis of peptic ulcer.

- Peptic ulcer is a complication of chronic gastritis.
- It is the result of a prolonged imbalance between the defensive and damaging forces of gastric mucosa and it arises when the damaging forces exceed the defensive ones.
- The pathogenesis of peptic ulcer is described below:



What are the main causes of duodenal ulcers?

- Duodenal ulcers are more frequent in individuals with:
 1. Alcoholic cirrhosis
 2. Chronic obstructive pulmonary disease (COPD)
 3. Chronic renal failure
 4. Hyperparathyroidism.
- In the last two conditions, *hypercalcaemia stimulates gastrin production* and therefore increases acid secretion.

What will be the morphology of the above specimen?

- The classic peptic ulcer is characterized by a *round to oval, sharply punched-out defect*.
- The mucosal margin is usually level with the surrounding mucosa.
- *Hemorrhage and fibrin deposition* are seen frequently.
- The *base of peptic ulcers is smooth and clean as a result of peptic digestion of exudate*.

- *In active ulcers the base is formed by [above to downwards: (Fig. 2.3)]*

1. A predominantly neutrophilic inflammatory infiltrate
2. A thin layer of fibrinoid debris
3. Immature granulation tissue
4. Fibrous tissue.

- Exposed blood vessels may be seen in the ulcer base, typically within the scarred area. The vessel walls are thickened and thrombus may be seen.

What are the complications of peptic ulcer?

1. Perforation and peritonitis: It is a medical emergency.
2. Hemorrhage (leading to hematemesis and melena).
3. Penetration of ulcer into the adjacent structures.
4. Obstruction (due to scar formation) leading to pyloric stenosis.
5. Malignant transformation (very rare).

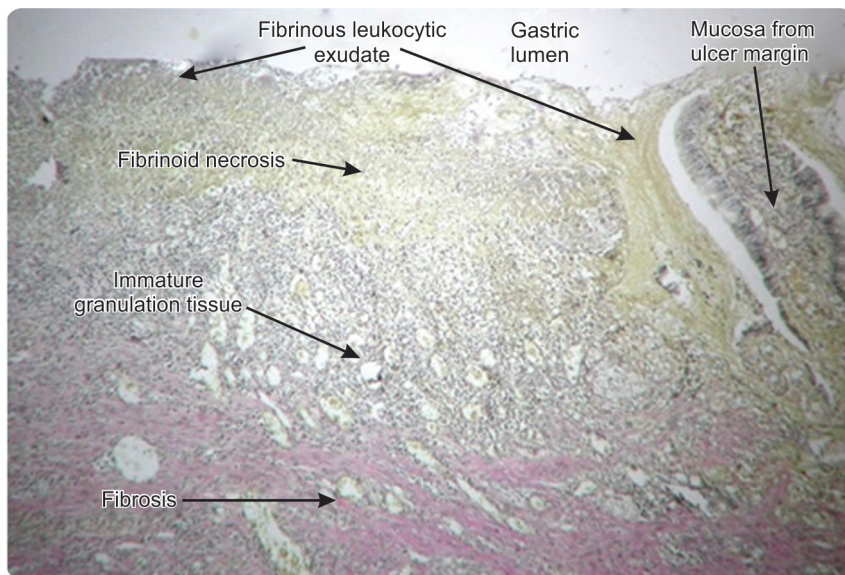


Fig. 2.3: Base of an active ulcer: Reproduced under the permission of Dr Mihai Danciu, Gr T Popa University of Medicine and Pharmacy, Iasi, Romania

What are the common clinical symptoms of peptic ulcer?

Usually the patients of peptic ulcer come to attention for the following clinical symptoms:

- Epigastric pain: Burning/continuous dull pain; often periodic
- Vomiting
- Bleeding
- Perforation and peritonitis (if complicated).

How can you diagnose peptic ulcer?

1. An upper GI endoscopy (preferably a gastroduodenoscopy) is considered to be the most accurate diagnostic test for peptic ulcer disease and considered to be the “Gold standard” for this purpose.
2. A urea breath test: It is based on the demonstration of ammonia produced by *H.pylori* from urea by the enzyme “Urease”.
3. A barium X-ray to detect any abnormality in the upper GIT (ulcer/ tumor/ hernia/ pouch/ stricture/ swallowing difficulty, etc.).

4. An ELISA test to detect antibodies against *H.pylori* in blood (has the disadvantage of getting a high numbers of false-positive reactions).

Can you name some drugs to treat peptic ulcer?

Two most effective triple drug regimens approved by FDA are:

1. Clarithromycin + Amoxicillin + Lansoprazole/Omeprazole (proton pump inhibitors).
2. Bismuth subsalicylate + Metronidazole + Tetracycline (BMT).

What is the relation between blood group and peptic ulcer?

Peptic ulcer is common among Group O persons.

Gastric carcinoma

Description

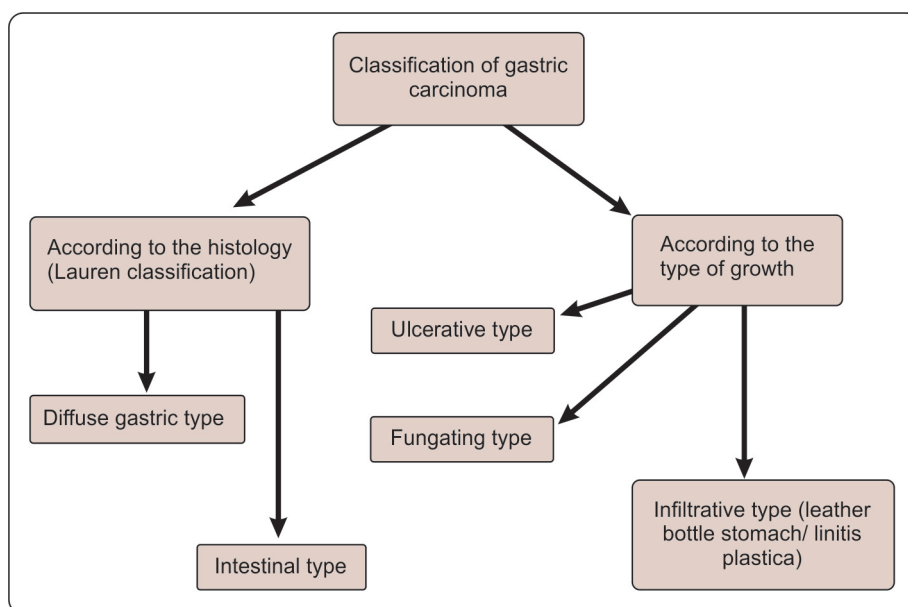
This is a specimen of stomach showing the following features (As shown in the following table) and the above specimen is identified as ‘Gastric carcinoma’ (Fig. 2.4).



Fig. 2.4: Gastric carcinoma

| Types | Description of the growth |
|---|---|
| Ulcerative type | Present on pylorus. Usually >3 cm in diameter, with thick and everted edge and hard indurated base formed by muscle |
| Fungating type | Large, cauliflower-like growth projecting in the lumen from mucosa, may cause pyloric obstruction when present in pylorus |
| Infiltrating type (leather bottle stomach) | Whole stomach is affected, length and cavity are grossly reduced, prominent mucosal fold and thickened wall |

What are the types of gastric carcinoma?



What is the pathogenesis of gastric carcinoma?

Pathogenesis of gastric carcinoma: Diffuse gastric type:

- E-cadherin is a protein that contributes to epithelial intercellular adhesion.
- Mutation in CDH1 gene (which codes E-cadherin) and subsequent loss of E-cadherin function seems to be a key step in the pathogenesis of diffuse gastric cancer.

Pathogenesis of gastric carcinoma: Intestinal type:

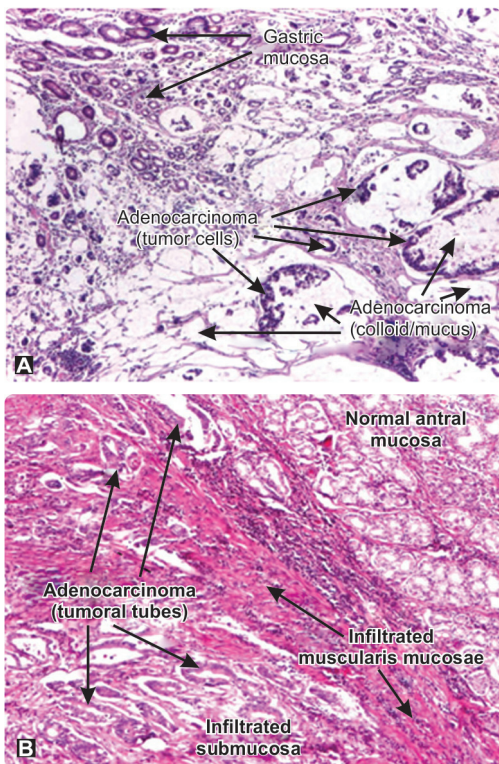
- Mutations/ microsatellite instability/ hypermethylation of various genes have been described in sporadic intestinal type gastric cancer:
 1. β -catenin
 2. TGFRII
 3. BAX
 4. IGFRII
 5. p16/INK4a.

What will be the morphology of the above specimen?

| Types of gastric CA | Diffuse gastric type | Intestinal type |
|---------------------|--|---|
| Features | | |
| Gross morphology | Diffuse infiltrative growth pattern | Bulky tumors, they typically grow along broad cohesive fronts to form an exophytic mass/an ulcerated tumor |
| Histology | They are generally composed of discohesive cells that do not form glands but instead have large mucin vacuoles that push the nucleus to the periphery, creating a <i>signet-ring cell morphology</i> (Fig. 2.5A) | They usually show a <i>glandular morphology</i> ; often associated with intestinal metaplasia of the surrounding area (Fig. 2.5B) |

It should be remembered at the very beginning that most of the gastric

carcinomas involve the gastric antrum and that the lesser curvature is involved more often than the greater curvature.



Figs 2.5 A and B: A. Morphology of diffuse type of gastric carcinoma: Presence of large amount of mucus and signet-ring cell morphology. B. Morphology of intestinal type of gastric carcinoma: Glandular morphology and intestinal metaplasia. Reproduced under the permission of Dr.Mihai Danciu, Gr T Popa University of Medicine and Pharmacy, Iasi, Romania

What is linitis plastica/ leather bottle stomach/ Brinton's disease/ diffuse stomach cancer?

It is a special type of stomach cancer characterized by involvement of the whole stomach, with a rigid and thickened wall caused by diffuse infiltration of the whole stomach by tumor cells and extensive fibrosis (Fig. 2.6).

Histologically, diffuse stomach cancer is characterized by a signet-ring cell morphology, caused by large mucin vacuoles pushing the nucleus to the periphery.



Fig. 2.6: Linitis plastica: Stomach opened longitudinally along the lesser curvature showing marked thickening of the gastric wall with mucosal congestion and decrease in rugal folds. Reproduced under the permission of Dr Andrew Ryan, MBBS, FRCPA

Which other cancers may create a linitis plastica appearance?

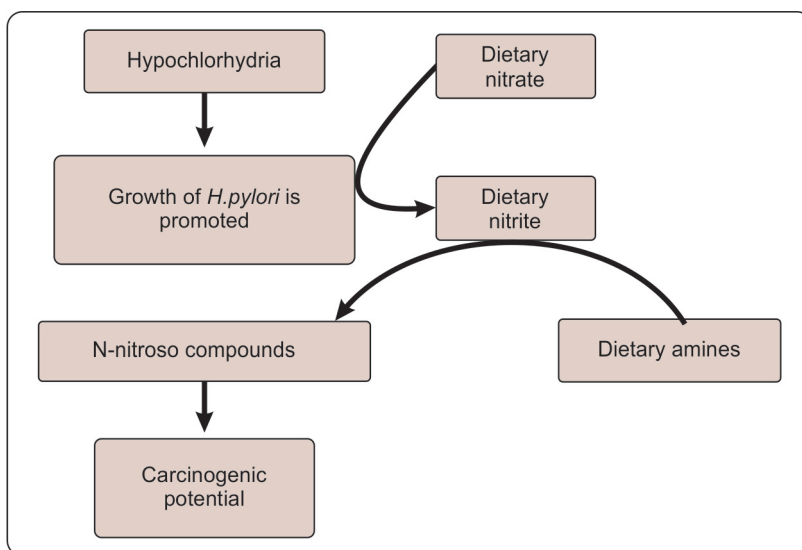
Breast and lung cancers that metastasize to the stomach may also create a linitis plastica-like appearance.

How hypochlorhydria helps in carcinogenesis?

- In presence of hypochlorhydria, the growth of *H.pylori* in stomach is promoted.
- This organism reduces dietary nitrate to nitrite.
- Then they convert the dietary amines to N-nitroso compounds (in the presence of nitrites).
- These N-nitroso compounds are highly carcinogenic and they are thought to be an important link between *H.pylori* and gastric cancer.

How can you differentiate between them?

| Points | Ulcer cancer | Cancer ulcer |
|--|---|--|
| Definition | It is malignant transformation of a pre-existing chronic peptic ulcer | It is ulceration of a previously existed carcinoma |
| Finding of an endoscopic biopsy from the corner along with the base of ulcer | Only 1 or 2 bits will show the evidence of carcinoma | All the bits will show the evidence of carcinoma |



Name some common risk factors for gastric carcinoma.

1. Hypochlorhydria
2. *H.pylori* infection
3. Intestinal metaplasia.

What is the difference between ulcer cancer and cancer ulcer?

What are the modes of spread of gastric carcinoma?

1. Local spread.
2. Metastasis to the supraclavicular lymph node (also called Virchow's node).
3. Metastasis to periumbilical region to form a subcutaneous nodule, termed as Sister Mary Joseph nodule.

4. Hematogenous spread to liver and lung.
5. Transcelomic spread to ovaries producing Krukenberg's tumor.

Small intestine

Tuberculous ulcer

Description

It is a specimen showing ulcer of the small intestine with:

| Features | Description |
|-------------|--|
| Long axis | Transversely disposed |
| Edge | Ragged and irregular |
| Floor | Showing small protuberances with no congestion of surrounding tissue |
| Serous coat | Showing presence of tubercles |

- So, the above specimen is identified as “Tuberculous ulcer of the small intestine” (Fig. 2.7).

What is the etiological origin of intestinal tuberculosis?

Intestinal TB is usually a form of secondary TB.

What are the various pathogenetic mechanisms of intestinal TB?

- Swallowing of infected sputum
- Dissemination of primary pulmonary tuberculosis
- Ingestion of nonpasteurized milk (contaminated with bovine tuberculosis).

Why TB ulcer is most common in terminal ileum and cecum?

1. TB ulcer occurs in the areas of Peyer's patches and lymphoid follicles. Both terminal ileum and cecum are very rich in both.
2. Movement of gut is sluggish in these parts, so bacteria gets more time to settle down here.

What are the different morphological types of tuberculous lesions found in the gut?



Fig. 2.7: Tuberculous ulcer

There are mainly 2 morphological types of intestinal TB:

- A. Ulcerative type
- B. Ulcerohypertrophic type.

It should be mentioned that there are no sharp differences between ulcerative and ulcerohypertrophic lesions and the two can occur at the same time.

| Types of the lesion | Features |
|-------------------------------|--|
| Ulcerative type (60%) | <ul style="list-style-type: none"> • Diseased areas are moderately indurated • Mesenteric fat is increased and mesenteric lymph nodes are enlarged • The circumference of the ulcer is studded with nodules of variable size • Characteristically, the established lesion consists of an <i>annular ulcer involving the entire circumference of a segment</i> and generally < 3 cm in length • The lumen in the affected region is markedly narrowed, often resulting in a stricture |
| Ulcerohypertrophic type (30%) | <ul style="list-style-type: none"> • Ulcerohypertrophic lesions usually affect the ileocecal region, the patient presenting with a large lump in the right iliac fossa • The ileocecal angle is distorted and often obtuse • <i>On opening, the wall is seen to be markedly thickened</i> (because of hypertrophy) • Mucosal changes are: <ol style="list-style-type: none"> a. Cobblestoning b. Pseudopolyposis c. Flattening of mucosal folds |

What are the common complications of a TB ulcer?

1. Acute or chronic obstruction from stricture, adhesions or both is the most common complication.
2. Perforation with peritonitis, usually in the ileum proximal to a stricture.
3. Fistulae between loops of bowel/ between the bowel and the skin/ between adjacent organs.
4. Malabsorption from lymphatic obstruction.

What are the clinical presentations of intestinal TB?

- Abdominal pain and distension

- Fever
- Diarrhea
- Weight loss
- Obstruction
- Melena (bleeding from upper GI tract)
- A palpable mass in the abdomen
- Anorexia
- Night sweats.

Why TB ulcers are uncommon nowadays?

The incidence of primary intestinal TB has become very rare nowadays primarily due to control of bovine TB by pasteurization of milk.

Typhoid ulcer

Description

- This is a specimen of small intestine wall.
- Centrally there is a well-circumscribed raised ovoid lesion in longitudinal alignment, interpreted as an ulcerated Peyer's patch (unlike in tuberculous ulceration, in which the ulcers are arranged with their long axes transverse to the length of the bowel).
- A similar small rounded lesion is present at the lower-end of the specimen and still smaller nodules are scattered throughout.

| Features | Description |
|-------------|--|
| Long axis | Oriented parallel to the long axis of the gut (longitudinally) |
| Shape | Oval |
| Edge | Regular, edematous, congested and raised |
| Floor | Pitted |
| Serous coat | Congested and having no tubercle |

- So, the specimen is identified as “Typhoid ulcer” (Figs 2.8 and 2.9).



Fig. 2.8: Typhoid ulcer of small intestine. Reproduced under the permission of Department of Clinical Laboratory Sciences, University of Cape Town, South Africa



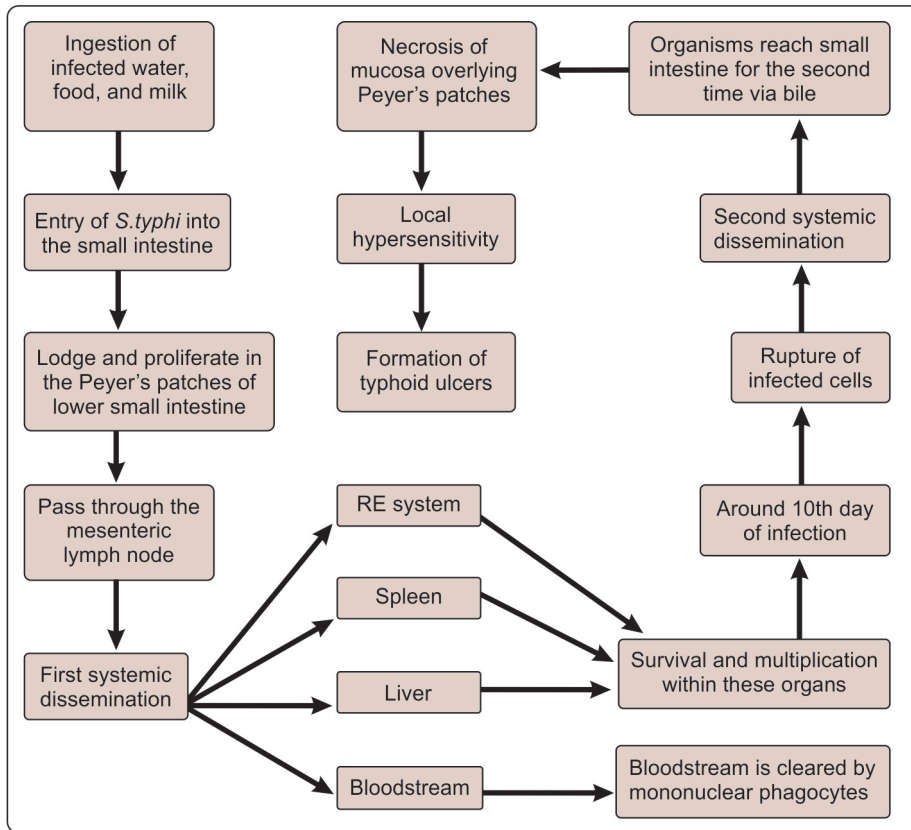
Fig. 2.9: Typhoid ulcer

What are the different phases of evolution of typhoid ulcer?

| Phases | Features |
|---------|---|
| Phase 1 | <i>Hyperplasia</i> of lymphoid follicles |
| Phase 2 | <i>Necrosis</i> of lymphoid follicles during the 2nd week involving both mucosa and submucosa |
| Phase 3 | <i>Ulceration</i> in the long axis of the bowel with the possibility of perforation and hemorrhage |
| Phase 4 | <i>Healing</i> takes place from the 4th week onward, and unlike tuberculosis of the bowel with its encircling ulcers, does not produce strictures |

Describe the pathogenesis of typhoid ulcer.

- After being ingested, the organism *Salmonella typhi* reaches the small intestine, penetrates the mucosa and carried to the Peyer's patches of the lower small intestine.



- Here they proliferate because of their special intracellular survival capability within the phagocytes and after passing through the mesenteric lymph nodes, they finally flood the bloodstream causing a systemic dissemination to the liver, spleen, and reticuloendothelial system.
- The bloodstream is immediately cleared by mononuclear phagocytes, but by the special capability of the organism mentioned above, they survive within these organs.
- By about 10th day of infection (varying from 1–3 weeks), the infected cells rupture and the bloodstream is flooded with large number of bacteria. This is the end of incubation period and the patient becomes seriously ill with septicemia.
- As the organisms reach the small intestine second time through bile, local hypersensitivity leads to necrosis of mucosa overlying Peyer's patches and results in formation of ulcer.

What is the most important histologic feature of a typhoid ulcer?

Presence of large number of macrophages, instead of neutrophils.

What is the most dangerous complication of a typhoid ulcer?

- In the 2nd or 3rd week of the illness, if the patient presents with severe generalized abdominal pain, it indicates a perforated typhoid ulcer.
- The patient will show classical features of peritonitis. (Abdominal pain, distension, fever, nausea, vomiting, loss of

appetite, diarrhea, thirst, low urine output, and constipation).

- So, any patient being treated for typhoid fever who shows a sudden deterioration accompanied by abdominal signs should be considered to have a typhoid perforation until proven otherwise.

What are the different lesions found in complicated typhoid fever?

| Organs | Lesion |
|--------------------|--|
| Intestine | Typhoid ulcer |
| Gallbladder | Cholecystitis |
| Liver | Typhoid nodules: Small, randomly scattered foci of parenchymal necrosis in which hepatocytes are replaced by macrophage aggregates |
| Spleen | Congestion and splenomegaly |
| Bones | Osteomyelitis |
| Skin | Typhoid rash |
| Respiratory system | Bronchitis and bronchopneumonia |
| Bone marrow | Suppression of leukopoiesis |
| Heart | Toxic myocarditis |
| CNS | Meningitis |

Large intestine

Colon carcinoma

Description

It is a specimen of proximal colon showing polypoid, exophytic masses that extend along one wall of the large-caliber cecum and ascending colon.

- So, this specimen is identified as colon carcinoma (Fig. 2.10).



Fig. 2.10: Carcinoma of colon. Specimen of a part of colon: Lower part of it is cut open to show a projecting fungating polypoid growth (arrows) with glistening surface

What is the pathogenesis of colon cancer?

The pathogenesis of colon carcinoma has 2 pathways:

- A. The classical adenoma-carcinoma sequence pathway (Fig. 2.11)
- B. The microsatellite instability pathway (Fig. 2.12).
 - Both are being discussed briefly here in diagrams.

What is the morphology of colon carcinoma?

1. The tumors are composed of tall columnar cells.
2. The invasive component of these tumors elicits a strong stromal desmo-

plastic reaction, which is responsible for the characteristic firm consistency of the tumor.

3. Glandular morphology with abundant mucin production is associated with poor prognosis.

What are the most common sites of metastasis?

- As a result of portal drainage of the colon, liver is the most common site of metastatic lesions.
- But metastases may also involve the following structures:
 1. Regional lymph nodes
 2. Lungs
 3. Bones.

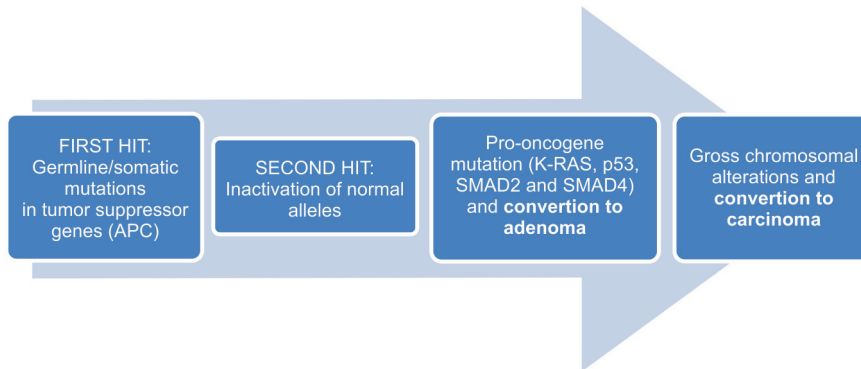


Fig. 2.11: The adenoma-carcinoma pathway

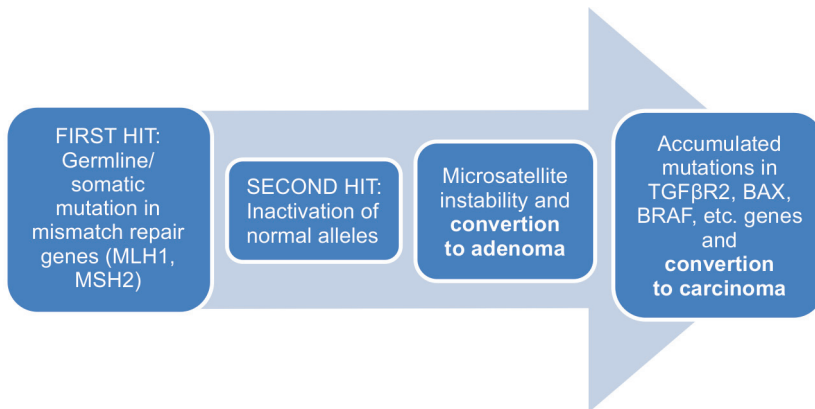


Fig. 2.12: The microsatellite instability pathway

What are the most common presenting features of colon carcinoma?

| <i>Colon cancers</i> | <i>Presenting features</i> |
|----------------------|---|
| Right-sided | Fatigue and weakness due to iron deficiency anemia |
| Left-sided | <ul style="list-style-type: none"> • Occult bleeding • Changes in bowel habits • Cramping left lower quadrant discomfort |

Is “Beta catenin” gene mutated in colon cancer?

- The “Beta catenin” commonly mentioned in CA colon is actually the Beta catenin protein, not the Beta catenin gene.
- Mutations in the APC gene in CA colon (the adenoma carcinoma sequence pathway) causes accumulation of Beta catenin protein within the cell cytoplasm, which leads to persistent activation of a transcription factor named TCF within the nucleus. Beta

catenin gene is never mutated in colon cancer.

- This causes abnormal cell proliferation and eventually leads to tumor formation.

In which cancers, the Beta catenin gene is actually mutated?

Mutations in Beta catenin gene are commonly associated with:

- a. Hepatoblastoma
- b. Hepatocellular carcinoma.

Name some of the genes which are mutated in colon cancer.

| <i>Types of colon cancer</i> | <i>Genes which are mutated</i> |
|------------------------------|--|
| Hereditary colon cancer | <ul style="list-style-type: none"> • APC • Mismatch repair genes |
| Sporadic colon cancer | <ul style="list-style-type: none"> • MYC • K-RAS • SRC • erbB2 • p⁵³ • APC • Mismatch repair genes |

CHAPTER

3

Liver

Basic histological anatomy of liver

It should be mentioned that the histopathology of liver is usually discussed on the basis of a lobular architecture. So, in the schematic diagram drawn below (Fig. 3.1):

- a. A lobule is oriented around the terminal hepatic vein (tributaries of hepatic vein).
- b. The area in the vicinity of terminal hepatic vein is called “Centrilobular” area (Fig. 3.2B).
- c. The area in the vicinity of portal tract is called “Periportal” area (Fig. 3.2A).

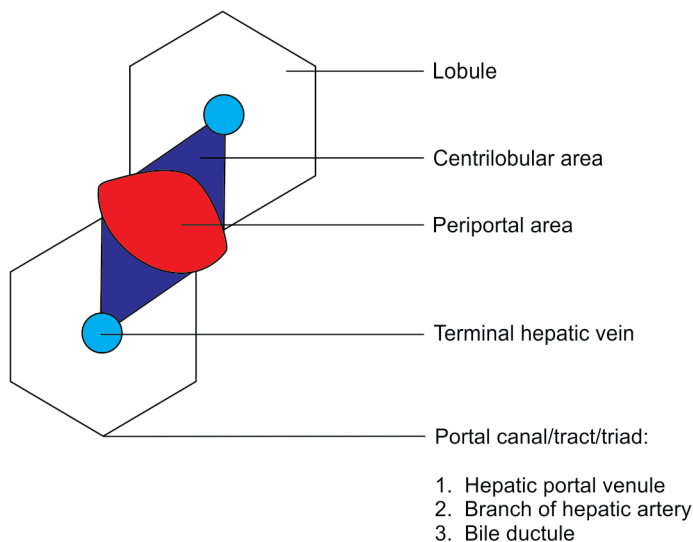
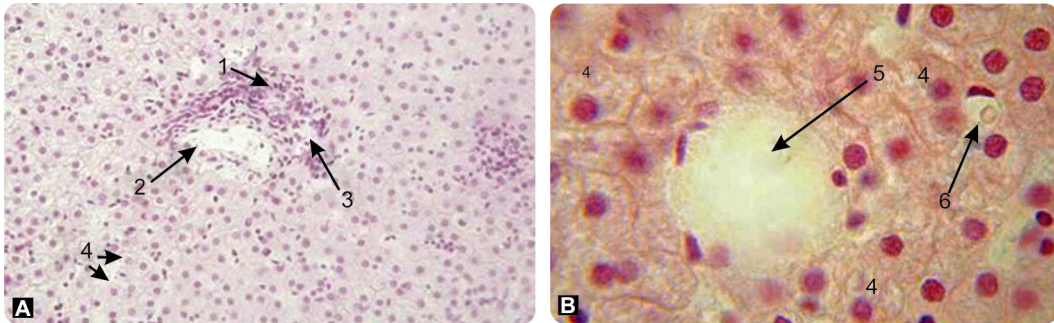


Fig. 3.1: Basic histopathological anatomy of liver



Figs 3.2A and B: Histological slides of liver stained with hematoxylin and eosin (H and E) showing A. Structure of a portal triad (1–Hepatic artery, 2–Portal vein, 3–Bile duct, 4–Hepatocytes) and B. Centrilobular area (4–Hepatocytes, 5–Terminal hepatic venule, 6–Hepatic sinusoid). Reproduced under the permission of Dr Andrei Gunin, Dept. of Histology, Chuvash State University, Russia

Fatty liver

Description

It is a specimen of liver tissue showing:

| Features | Description |
|-------------|--------------------|
| Color | Pale yellow |
| Surface | Smooth |
| Capsule | Stretched |
| Margin | Rounded |
| Cut surface | Greasy (if fresh) |
| Consistency | Soft (if palpated) |

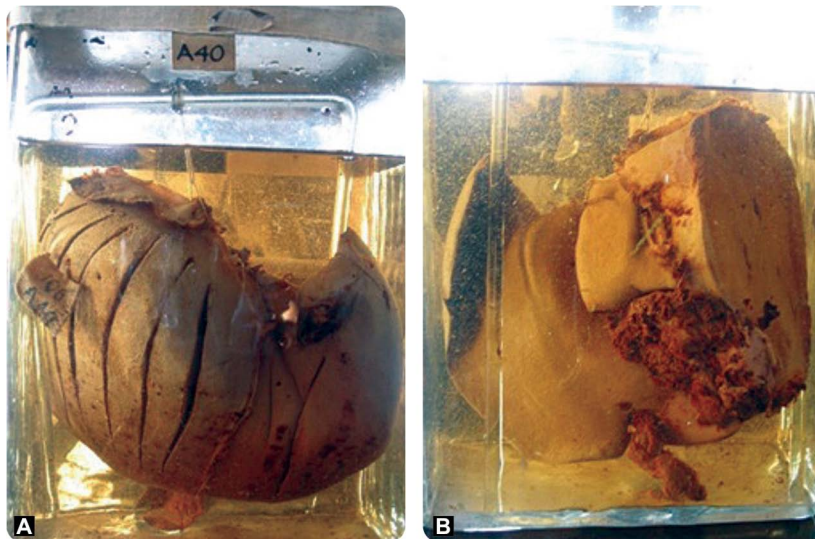
- So, the above specimen is identified as “Fatty liver” (Figs 3.3A and B).

What do you mean by “Fatty liver”?

Fatty liver is a reversible condition where large vacuoles of triglyceride (TAG) accumulate within the hepatocytes.

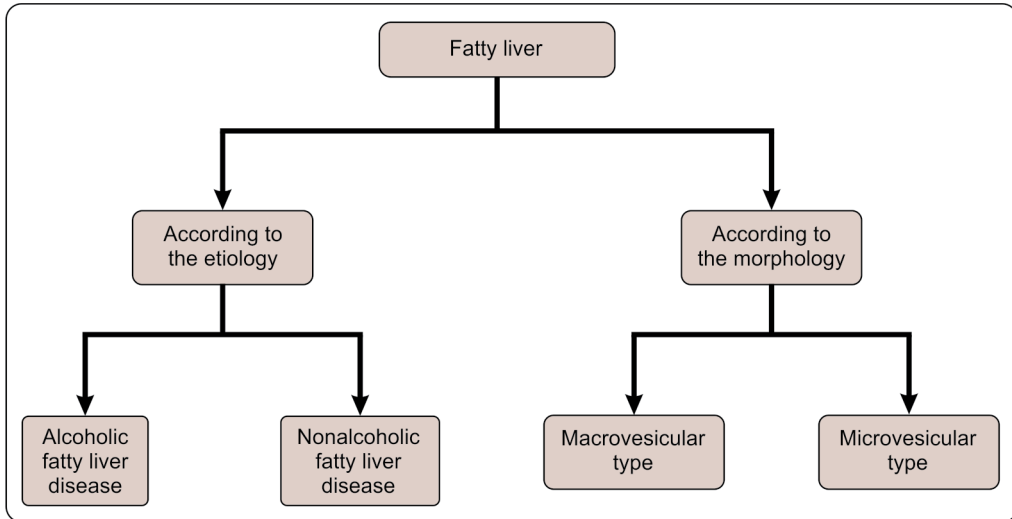
What do you mean by “Steatosis”?

“Steatosis” is defined as abnormal retention of fat within a cell.

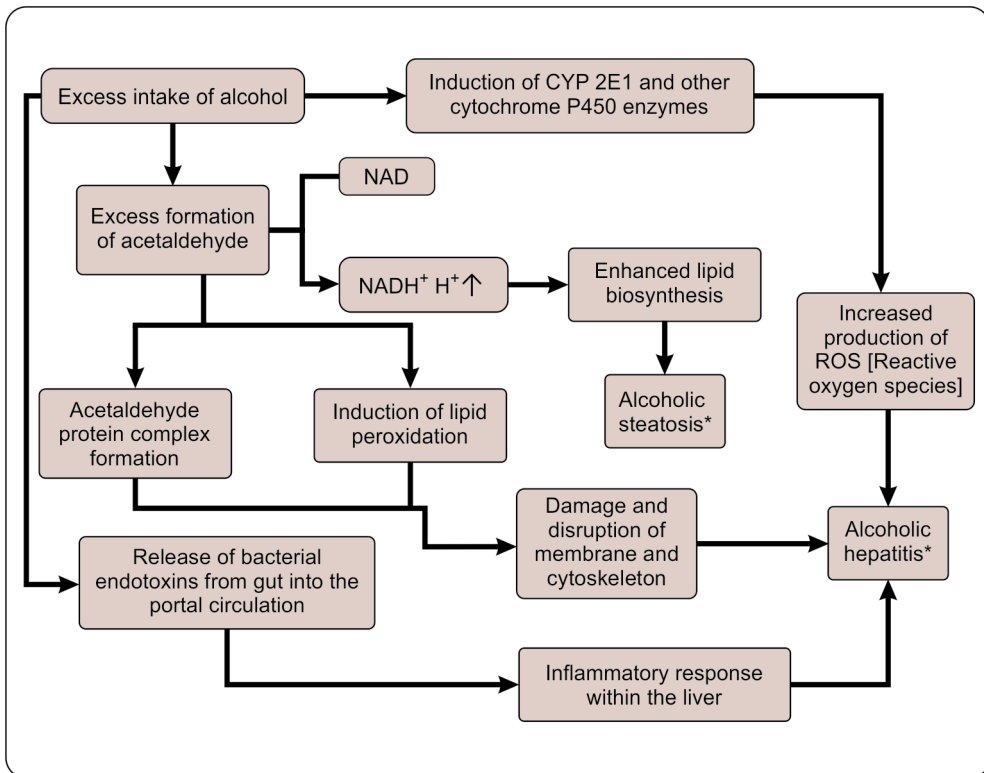


Figs 3.3A and B: Fatty liver. A. Front view and B. Back view

How can you classify fatty liver?



Describe the pathogenesis of alcoholic fatty liver disease/alcoholic steatosis.



(*These 2 processes are together termed as "Alcoholic steatohepatitis").

What are the different pathologic stages in the progression of alcoholic steatohepatitis?

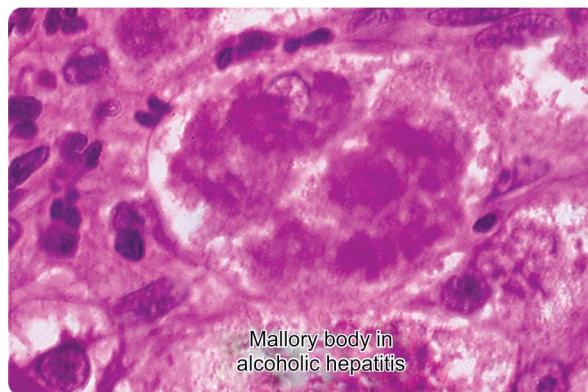
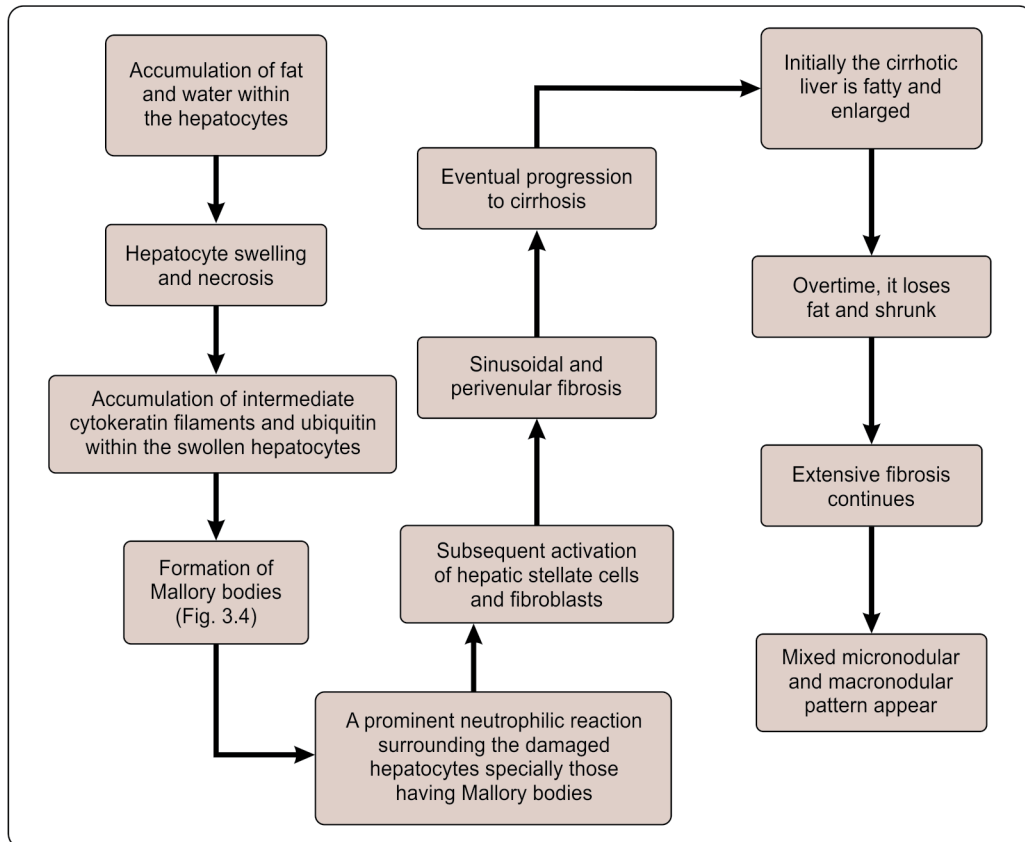
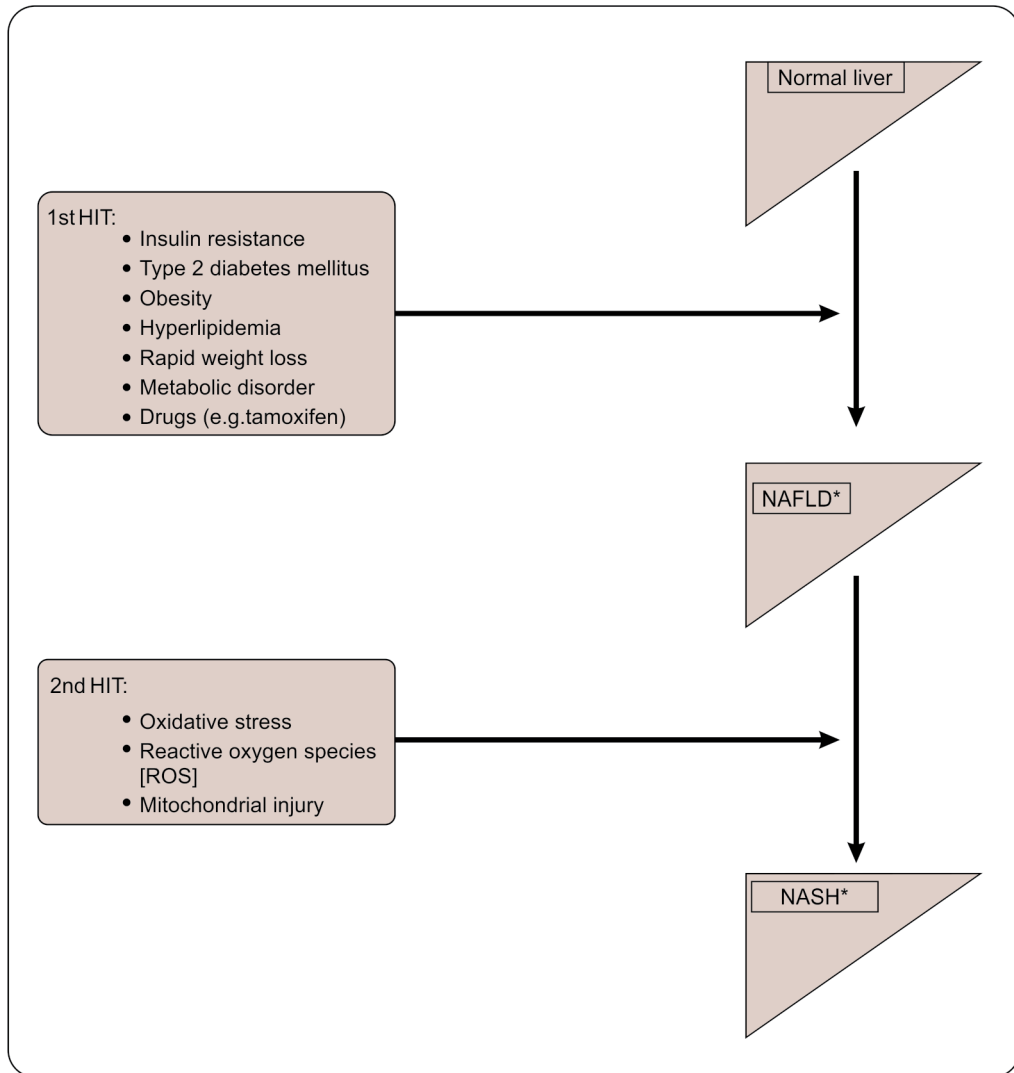


Fig. 3.4: Micrograph showing a Mallory body at the center of the image within a swollen hepatocyte. As they are highly eosinophilic in nature, they appear pink in H and E stain. (Reproduced under the permission of Joel Greenon, University of Michigan)

Describe the pathogenesis of nonalcoholic fatty liver disease (NAFLD).

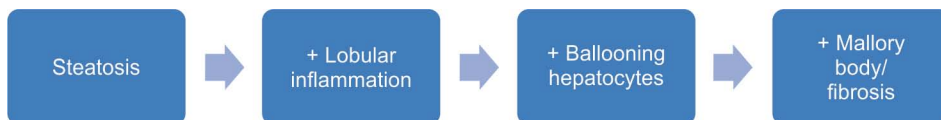


The pathogenesis of NAFLD is not entirely known, but a “2 Hit hypothesis” model has been proposed to describe it. The 2 Hits are:

- 1st Hit: Hepatic fat accumulation
- 2nd Hit: Oxidative stress on liver.

(*NAFLD: Nonalcoholic fatty liver disease and NASH: Nonalcoholic steatohepatitis).

What are the different pathologic stages in the progression of NAFLD?



Further reading: NAFLD activity score (NAS score) and fibrosis staging:

| <i>Item</i> | <i>Score</i> | <i>Extent</i> |
|---|--------------|------------------------------------|
| Steatosis (Surface area involved by steatosis) | 0 | <5% |
| | 1 | (5–33)% |
| | 2 | (34–66)% |
| | 3 | >66% |
| Lobular inflammation (No. of focus per 200X) | 0 | No foci |
| | 1 | <2 foci |
| | 2 | 2–4 foci |
| | 3 | >4 foci |
| Hepatocyte ballooning | 0 | None |
| | 1 | Few cells |
| | 2 | Many cells/prominent ballooning |
| Fibrosis (Evaluated separately from NAS score) | 0 | None |
| | 1 | Perisinusoidal/periportal |
| | 2 | Perisinusoidal + periportal/portal |
| | 3 | Bridging fibrosis |
| | 4 | Cirrhosis |

(A NAS score of 0–2: Not diagnostic of NASH; 3–4: Marginal and 5–8 is considered diagnostic of NASH).

What is the morphological classification of fatty liver and give some of the causes of each?

| <i>Morphological types</i> | <i>Description</i> | <i>Common causes</i> |
|----------------------------|--|---|
| Macrovesicular fatty liver | Intracellular lipid droplets with diameter $\geq 25 \mu\text{M}$, shifting the nucleus to the periphery, usually single | <ul style="list-style-type: none"> • Obesity • Type 2 diabetes mellitus • Alcohol • Steroids • Kwashiorkor • Wilson's disease |
| Microvesicular fatty liver | Intracellular droplets with diameter 3–5 μM , often multiple | <ul style="list-style-type: none"> • Acute fatty liver of pregnancy • Viral hepatitis • Drugs (Salicylate/Tetracycline) |

Describe the histology of fatty liver.

- Section showing histology of liver tissue with normal architectural pattern.
- Hepatocytes are showing large clear vacuoles in the cytoplasm (Fig. 3.5).
- Nucleus has been pushed to the periphery by the cytoplasmic vacuole, to give the hepatocytes a resemblance to signet-ring. So, this morphology is known as “signet-ring appearance”.

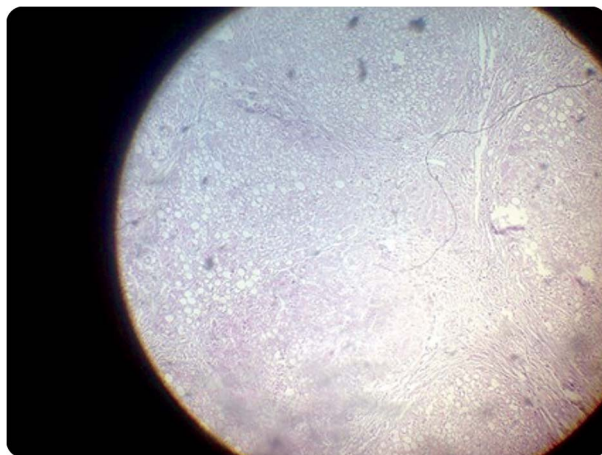


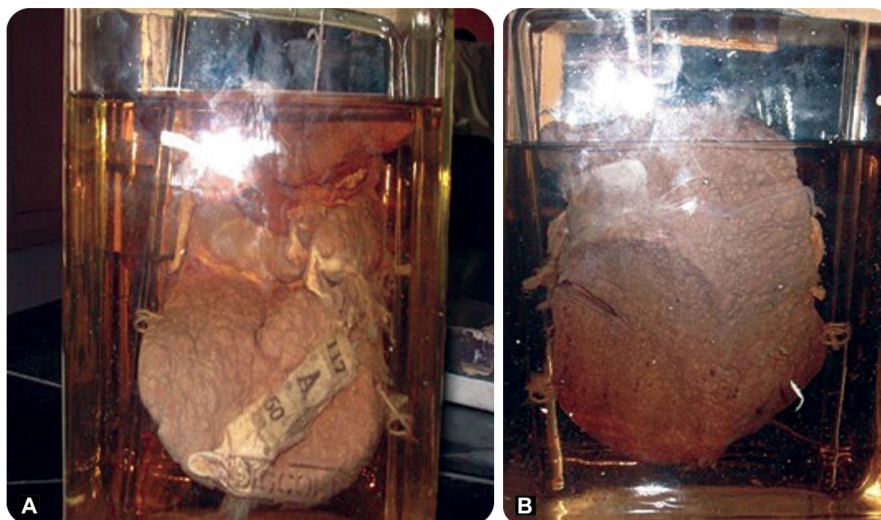
Fig. 3.5: Histology of fatty liver. Hepatocytes are showing clear vacuoles within the cytoplasm: Architectural pattern of tissue is preserved

Cirrhosis of liver

Description

This is a specimen of intact liver showing the following features (As shown in the following table) and the specimen is identified as “Cirrhosis of liver” (Figs 3.6A and B).

| Features | Description |
|----------|---|
| Color | Yellowish orange |
| Surface | Nodules of variable size alternating with depressed areas |
| Size | Shrunken |
| Margin | Sharp |



Figs 3.6A and B: Cirrhosis of liver. A. Front view and B. Back view

What do you mean by cirrhosis/define cirrhosis?

WHO definition of cirrhosis:

Cirrhosis is defined as a diffuse process characterized by fibrosis and the conversion of normal liver architecture into structurally abnormal nodules.

What are the criteria for diagnosis of cirrhosis?

1. **Parenchymal nodules:** They contain scattered foci of living hepatocytes surrounded by zones of fibrosis; resulting from repeated cycles of hepatocyte regeneration and scarring.

These are of two types:

- A. If the diameter is <3 mm, then it is called "Micronodule".
- B. If the diameter is >3 mm, then it is called "Macronodule".

So, according to the presence of nodules, cirrhosis can be morphologically divided into 3 types:

A. Micronodular pattern:

- Abundant micronodules are found.
- The striking feature is the regularity in the nodule size.
- Generally they don't contain any normal structures within them (like portal tract/efferent vein, etc.).

B. Macronodular pattern:

- Abundant macronodules are found.
- The nodule size is variable.
- They may contain normal hepatic structures (portal tract/efferent vein, etc.).

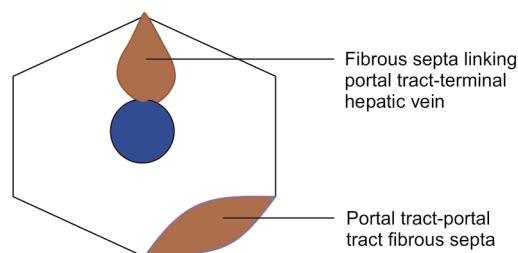
C. Mixed pattern:

- When micronodules and macronodules are present in

approximately equal proportions, the term "Mixed" is used.

2. **Bridging fibrous septa:** These are mainly of 2 types:

- A. Linking one portal tract to another
- B. Linking portal tracts with terminal hepatic veins.



3. **Disorganization of the lobular architecture of the entire liver:** As cirrhosis is an irreversible and terminal stage of chronic liver diseases, it is characterized by diffuse involvement of the liver, comprising of:

- A. Diffuse parenchymal injury and necrosis
- B. Diffuse fibrosis.

What is the basis of nodule formation in cirrhosis?

Throughout the process of liver damage and fibrosis in the development of cirrhosis, the surviving hepatocytes are stimulated to regenerate and proliferate as spherical nodules within the confines of the fibrous septa.

What is the basis of depressions found in cirrhotic liver?

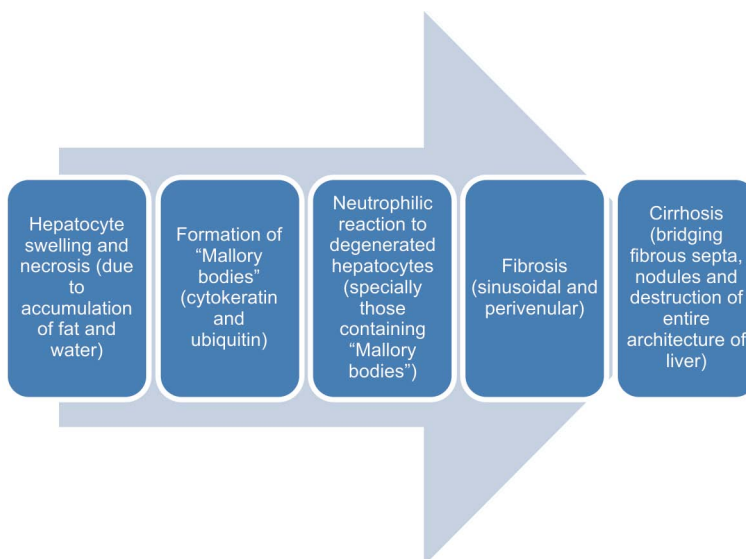
The alternating depressions occur due to contraction of fibrous bands and atrophy of hepatocytes.

Can you name some etiological factors associated with cirrhosis of liver?

| <i>Etiological association</i> | <i>Etiological factors</i> |
|--------------------------------|---|
| Established | <ul style="list-style-type: none"> • Viral hepatitis • Alcoholic and nonalcoholic fatty liver disease • Primary biliary cirrhosis • Secondary biliary cirrhosis • Metabolic disorders: <ul style="list-style-type: none"> – Wilson's disease – Hemochromatosis – α_1-antitrypsin deficiency, etc. • Drugs: <ul style="list-style-type: none"> – Methotrexate – α-methyl dopa |
| Debatable | <ul style="list-style-type: none"> • Autoimmunity • Malnutrition • Schistosomiasis |
| Unknown | <ul style="list-style-type: none"> • Indian childhood cirrhosis • Cryptogenic cirrhosis |

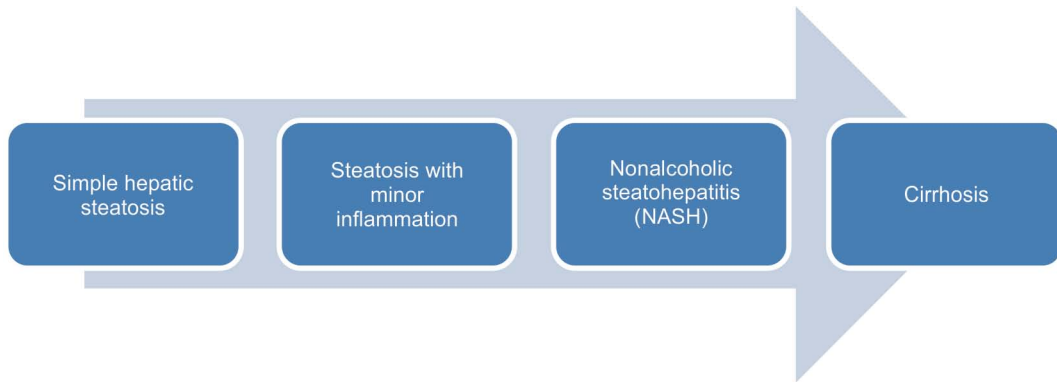
Here, we are discussing the pathogenesis of some of the important well-established etiological factors that are responsible for cirrhosis:

1. **Viral hepatitis (Type B, C, D):** These viruses are responsible for cirrhosis of liver in a background of chronic hepatitis; which is associated more with hepatitis C virus; although hepatitis B and hepatitis D viruses (Hepatitis D is active only in the presence of Hepatitis B virus) cause a substantial number of liver cirrhosis.
2. **Alcoholic fatty liver disease (AFLD)/ Alcoholic steatohepatitis (ASH):** Cirrhosis is the final and irreversible outcome. The successive stages are:



3. **Nonalcoholic fatty liver disease (NAFLD):** It occurs in persons who don't consume alcohol. It should be remembered that the histological

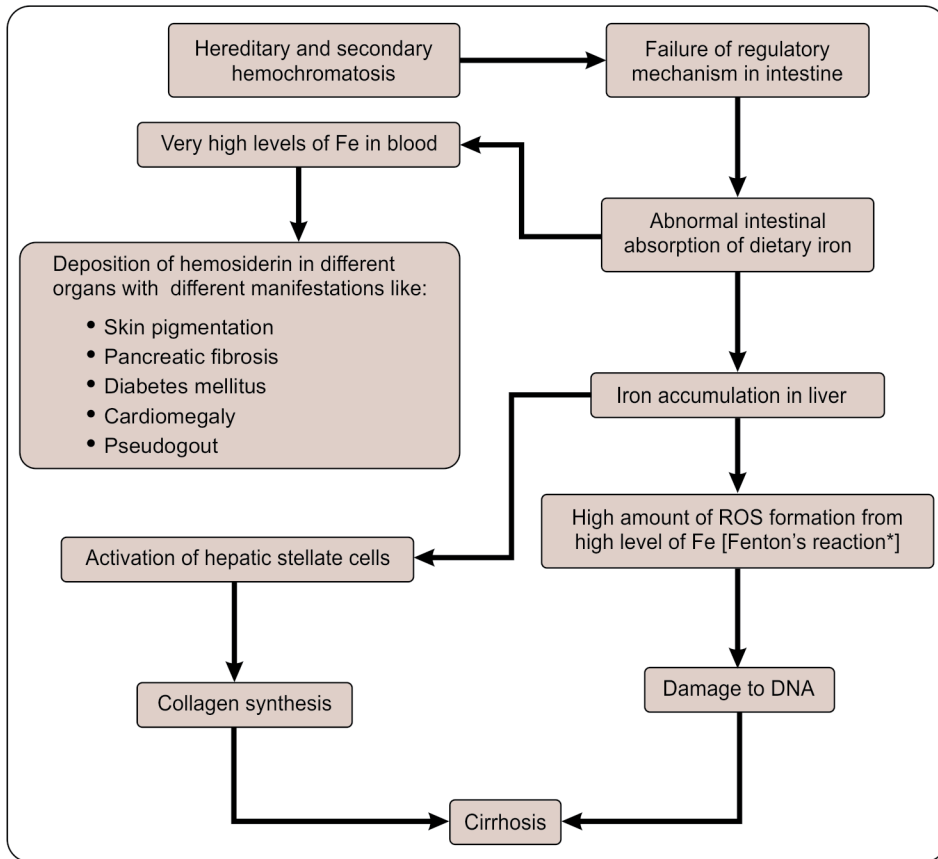
features of NASH (nonalcoholic steatohepatitis) are same as ASH (alcoholic steatohepatitis) and in both; cirrhosis is the final outcome.



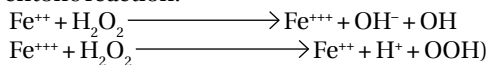
4. **Hemochromatosis:**
It is of 2 types:

- i. Hereditary
- ii. Secondary.

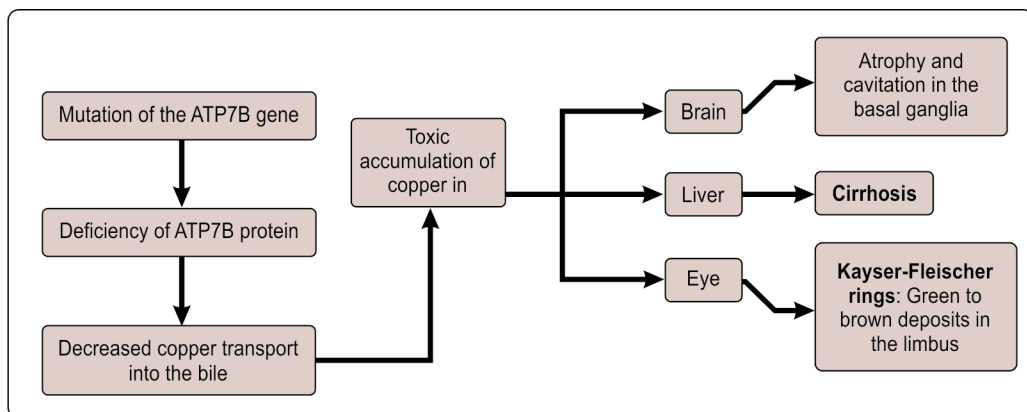
| <i>Types of hemochromatosis</i> | <i>Causes</i> |
|---|--|
| Hereditary hemochromatosis | Mutations in: <ul style="list-style-type: none"> • Transferrin receptor • Hpcidin |
| Secondary hemochromatosis/Hemosiderosis/ Secondary iron overload | <ul style="list-style-type: none"> • Transfusion • Long-term dialysis • Aplastic anemia • Sickle cell disease • Beta-thalassemia • Sideroblastic anemia • Chronic liver disease |



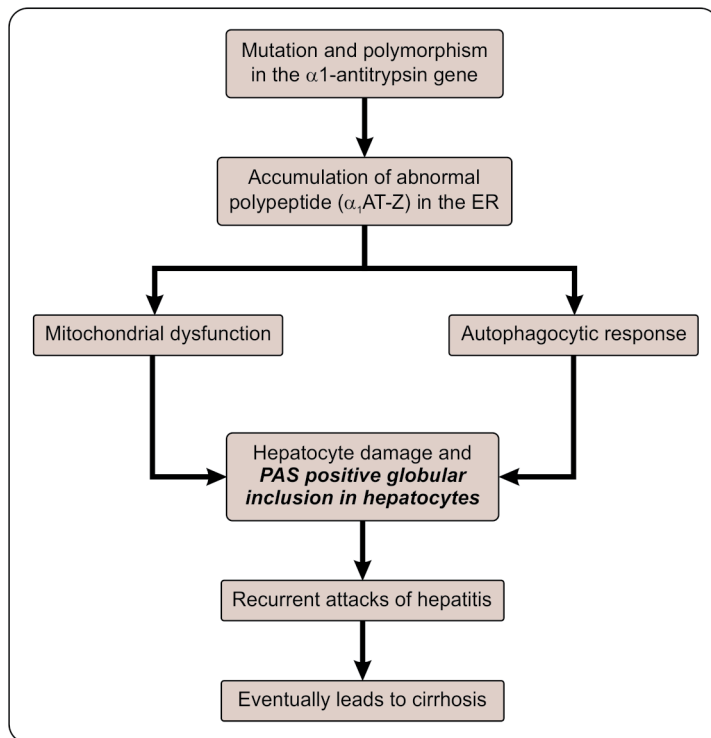
(* Fenton's reaction:



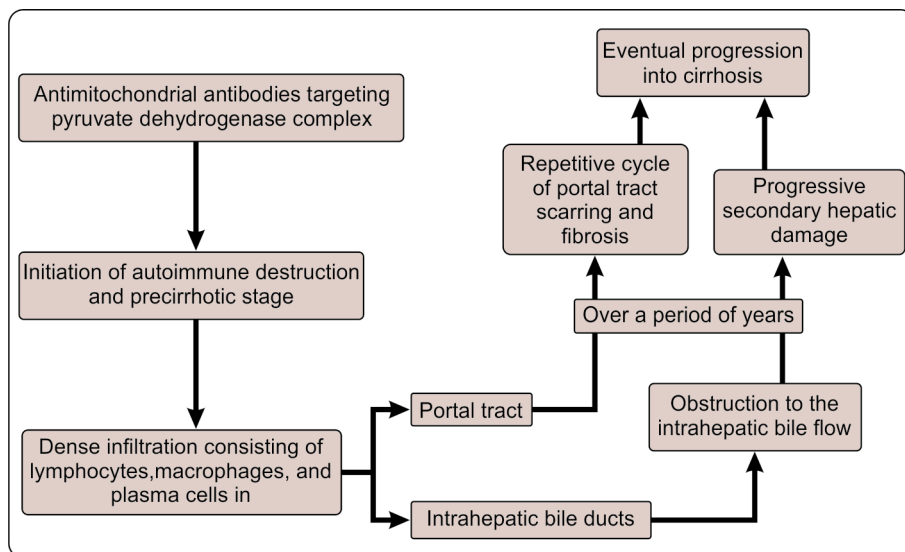
5. Wilson's disease:

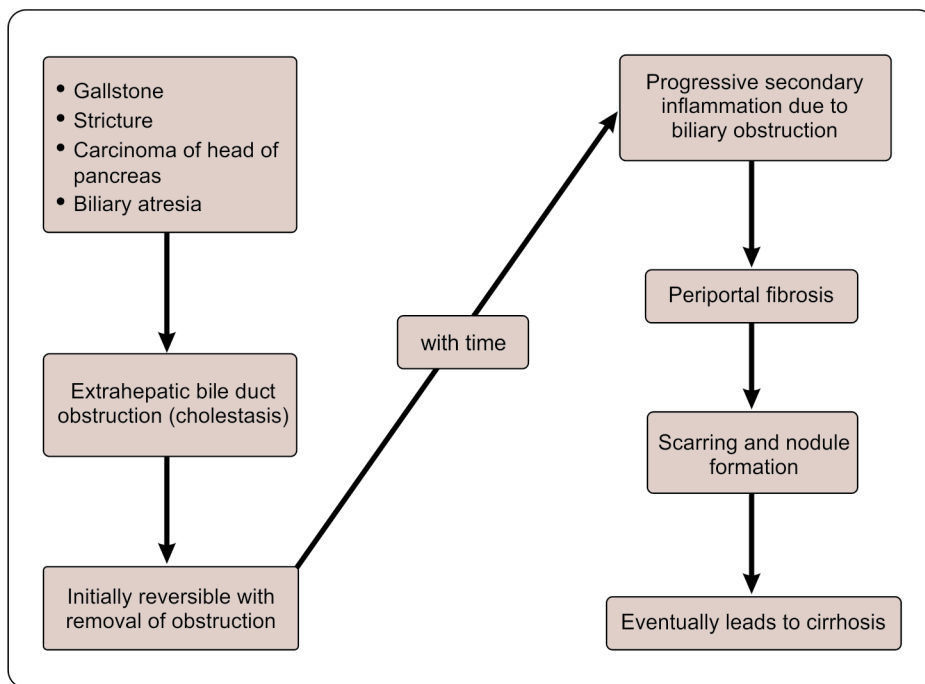


6. α_1 -antitrypsin deficiency (Predominantly seen in children):



7. Primary biliary cirrhosis (PBC):



8. **Secondary biliary cirrhosis (SBC):****Mention the complications of cirrhosis.**

| <i>Causes</i> | <i>Complications</i> |
|---|---|
| Due to portal obstruction and portal hypertension | <ul style="list-style-type: none"> • Ascites • Splenomegaly • Esophageal varices/caput medusa |
| Due to hepatocyte damage | <ul style="list-style-type: none"> • Coagulation defect • Macrocytic anemia • Hypoproteinemia: Edema and ascites • Malignant transformation to hepatocellular carcinoma |

What are the causes of bleeding in portal cirrhosis?

1. Due to portal hypertension, rupture of anastomotic vessels occurs.

2. Coagulation defect due to deficiency of coagulation factors.

What are the causes of death in portal cirrhosis?

1. Secondary infection
2. Hemorrhage
3. Hepatic coma
4. Acute pulmonary edema.

Metastatic carcinoma of liver

Description

- It is a specimen of cut section of liver showing multiple, large, and nodular growths.
- The nodules are yellowish white in color.
- Central parts of many nodules are depressed (umbilication).
- There are blackish areas of hemorrhage and areas of cystic changes.
 - So, the specimen is identified as

“Metastatic carcinoma of liver”
(Figs 3.7A and B).

Why this is not a specimen of cirrhosis?

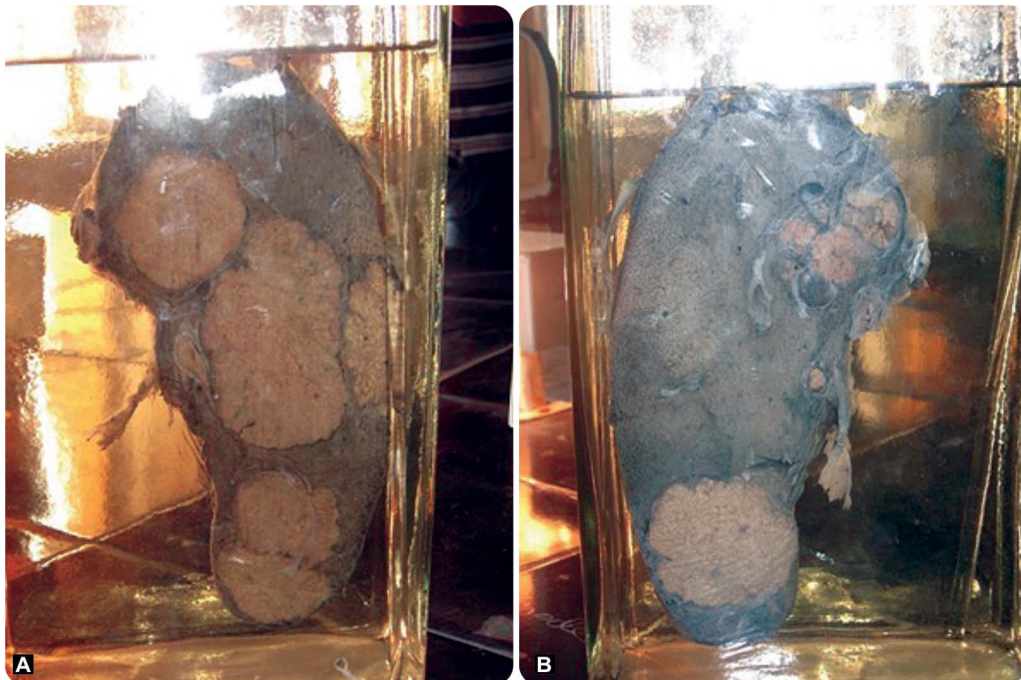
Because in cirrhosis:

- The nodules are surrounded by fibrous bands.
- Nodules are smaller and never show umbilication.
- Usually no areas of hemorrhage/ necrosis are seen in cirrhosis.

Why this is not a specimen of hepatocellular carcinoma?

Because in hepatocellular carcinoma:

- The growth is usually solitary and massive.
- Umbilication is absent.
- Surrounding liver tissue is usually cirrhotic.



Figs 3.7A and B: Metastatic carcinoma of liver. A. Front view and B. Back view

What are the sources of metastasis in this specimen?

| <i>General route</i> | <i>Description of spread</i> |
|-----------------------|---|
| Direct invasion from | <ul style="list-style-type: none">• Gallbladder• Head of pancreas• Hepatic flexure of colon |
| Lymphatic spread from | <ul style="list-style-type: none">• Stomach• Breast |
| From portal vein | <ul style="list-style-type: none">• Stomach• Colorectal areas of gut (most common)• Small intestine |
| From hepatic artery | <ul style="list-style-type: none">• Kidney• Bones• Uterus• Thyroid |

CHAPTER

4

Kidney

Large white kidney

Description

- Kidney is enlarged
- Color of the specimen is pale/white
- Surface is smooth
- Capsule is thin.



Fig. 4.1: Large white kidney

- So, the above specimen is identified as “Large white kidney” (Fig. 4.1).

[Note: Capsule may easily be stripped off, consistency is soft.]

What are the common causes of large white kidney?

1. Rapidly progressing glomerulonephritis (RPGN): Most common cause.
2. Membranous glomerulonephritis.
3. Membranoproliferative glomerulonephritis.
4. Amyloid kidney.

Why is the kidney large and white?

- **Large:** Due to edema.
- **White:** Due to associated vascular compression.

Describe the histology of RPGN.

- The histologic picture is dominated by distinctive **crescents** (Fig. 4.2).
- Crescents are formed by proliferation of parietal cells and by migration of monocytes and macrophages into the urinary space.
- Eventually, most crescents undergo sclerosis.

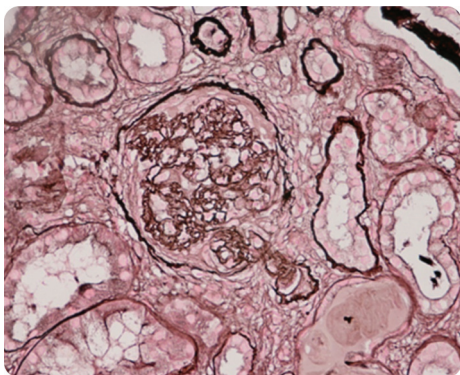


Fig. 4.2: Photomicrograph of a renal biopsy specimen showing crescent formation and tuft narrowing; Jones' stain. Reproduced under the permission of Dr Ramaswami, Nephrologist, Queensland, Australia

What is the role of fibrin in the formation of crescents in RPGN?

Fibrin strands are frequently prominent between the cellular layers in the crescents; and it is thought that the escape of fibrinogen into Bowman space and its conversion to fibrin are an important contributor to crescent formation.

What are the different types of RPGN? Give 1 example of each.

There are 3 types of RPGN:

| Types of RPGN | Examples |
|--|-----------------------------------|
| Anti GBM antibody induced disease (Type 1) | Goodpasture syndrome |
| Immune complex mediated RPGN (Type 2) | Postinfectious glomerulonephritis |
| Pauci immune type RPGN (Type 3) | Wegener granulomatosis |

What are the immunofluorescence findings of different types of RPGN?

| Types of RPGN | Immunofluorescence findings |
|--|-----------------------------|
| Anti GBM antibody induced disease (Type 1) | Linear deposits of IgG |

Contd...

| Types of RPGN | Immunofluorescence findings |
|---------------------------------------|--|
| Immune complex mediated RPGN (Type 2) | Granular immune deposits |
| Pauci immune type RPGN (Type 3) | Little/ no deposits of anti GBM antibodies/ immune complex |

What is the danger of RPGN?

RPGN is associated with rapid deterioration of renal function and if not immediately, death from renal failure may occur within weeks to months.

Other important questions that may be asked from this point

What are the findings of light microscopy/ immunofluorescence/electron microscopy of poststreptococcal glomerulonephritis (PSGN).

| Diagnostic procedures | Findings |
|-----------------------|--|
| Light microscopy | Enlarged and hypercellular glomeruli |
| Immunofluorescence | Granular deposits of IgG, IgM, and C ₃ in the mesangium and along the GBM |
| Electron microscopy | Discrete electron-dense deposits on the epithelial side of the membrane |

What is the cause of hypercellularity found in the light microscopy in case of poststreptococcal GN?

The hypercellularity in poststrep GN is caused by:

- A. Proliferation of epithelial and mesangial cells
- B. Infiltration of neutrophils and monocytes.

Contd...

What are the manifestations of nephrotic syndrome and what are the causes of these manifestations?

| Manifestations | Causes |
|--|---|
| Massive proteinuria (daily loss of protein is ≥ 3.5 gm) | Damage to the glomerular capillary walls resulting in increased permeability to plasma proteins |
| Hypoalbuminemia (plasma albumin level is < 3 gm/dL) | Loss of large portions of albumin through the urine |
| Generalized edema | <ul style="list-style-type: none"> Decreased colloid osmotic pressure (COP) of the blood with subsequent accumulation of fluid in the interstitial tissues Sodium and water retention |
| Hyperlipidemia and lipiduria | <ul style="list-style-type: none"> Increased synthesis of lipoproteins in the liver Decreased catabolism of lipids |

Name some genes which, when mutated, may lead to nephrotic syndrome?

| Name of the gene | Name of the coded protein | Name of the nephrotic syndrome |
|------------------|---------------------------|---|
| NPHS1 | Nephrin | Congenital nephrotic syndrome: Finnish type |
| NPHS2 | Podocin | Steroid resistant nephrotic syndrome: Childhood onset |

Name some common causes of nephrotic syndrome.

| Causes | Examples |
|-----------------------------|---|
| Primary glomerular diseases | <ul style="list-style-type: none"> Minimal change disease Focal segmental glomerulosclerosis (FSGS) Membranous nephropathy Membranoproliferative glomerulosclerosis* IgA nephropathy |
| Systemic diseases | <ul style="list-style-type: none"> Diabetes mellitus SLE Amyloidosis Malignancy Infections (mainly STDs like HIV, HBV, syphilis) |

(* often has mixed nephritic/nephrotic syndrome)

What is the most frequent cause of nephrotic syndrome in children? What is its characteristic histological feature? Why the prognosis is usually good?

- Minimal change disease; it is commonly seen in children of 2–6 years of age.
- The most characteristic histological feature is diffuse effacement of foot processes of visceral epithelial cells (podocytes) in glomeruli, which is visible only in electron microscopy.

- The most striking feature is that the glomeruli in minimal change disease appear almost normal when seen in light microscopy.
- The prognosis is excellent because of its dramatic response to corticosteroid therapy.

What do you mean by focal segmental glomerulosclerosis (FSGS)?

- Focal:** Only some of the glomeruli are involved.

- **Segmental:** In the affected glomeruli, only a portion of the capillary is involved.
- **Glomerulosclerosis:** The change in the glomeruli is mainly sclerosis.

What do you mean by hyalinosis and sclerosis?

- **Hyalinosis:** Extracellular deposition/ entrapment of plasma proteins into the glomerular structures.
- **Sclerosis:** Accumulation of extracellular collagenous matrix (ECM) in the mesangium/ capillary loops.
 - They are common features of FSGS.

Shortly tell the pathogenesis and specific findings in membranous nephropathy and membranoproliferative glomerulonephritis (MPGN).

Name the characteristic changes in the diabetic nephropathy.

1. Glomerular lesions:
 - a. Capillary basement membrane thickening.
 - b. Diffuse mesangial sclerosis.
 - c. Nodular glomerulosclerosis (with fibrin caps and capsular drops).
2. Hyaline arteriosclerosis of the afferent and efferent arteriole.
3. Acute pyelonephritis (papillary necrosis).

What is the similarity of IgA nephropathy and renal manifestation of Henoch-Schönlein purpura? What is the conclusion from this similarity?

- In both of the diseases, IgA is deposited in the glomerular mesangium.
- This has led to the concept that IgA

| Diseases | Pathogenesis | Light microscopy | Fluorescence microscopy | Electron microscopy |
|------------------------|--|--|--|---------------------------------------|
| Membranous nephropathy | Immune complex formation in glomerulus | Uniform and diffuse thickening of glomerular capillary wall | Granular deposits (C_3 + IgG) | Subepithelial electron-dense deposits |
| MPGN type 1 | Immune complex in glomerulus; activation of both classical and alternative complement pathways | The large and hypercellular glomeruli show "lobular" appearance due to the proliferating mesangial cells and increased proliferation of mesangial matrix | Granular deposits (C_3 + IgG; C1q + C_4) | Subendothelial deposits |
| MPGN type 2 | Activation of alternative complement pathway only | Glomerular capillary wall shows "Tram track appearance", due to duplication of GBM | Granular/linear deposits (C_3 ± IgG) | Dense deposits in the GBM |

Name the glomerulopathy most commonly seen in patients of HIV.

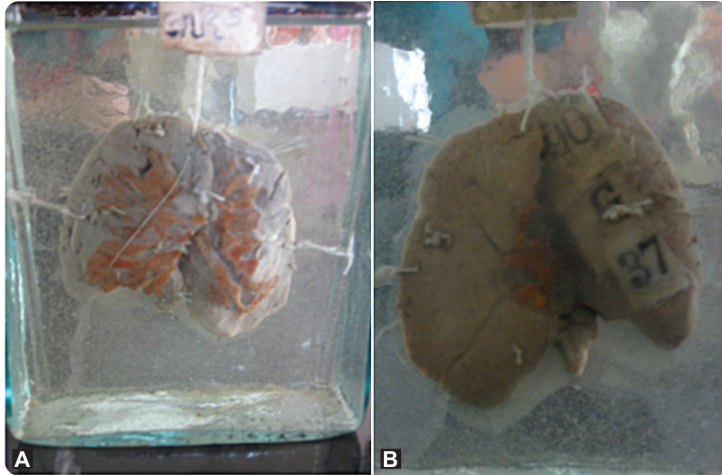
- Collapsing glomerulopathy; it is a morphologic variant of FSGS (focal segmental glomerulosclerosis).
- The pathogenesis of HIV-related FSGS is thought to be due to infection of glomerular and tubular cells by HIV.

nephropathy and HS purpura are both manifestations of the same disease.

Granular contracted kidney

Description

- Size of kidney is grossly reduced.
- Surface is finely granular.



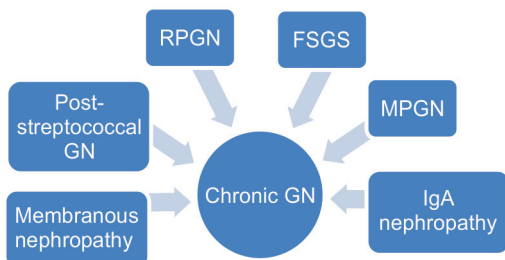
Figs 4.3A and B: Granular contracted kidney. A. Front view and B. Back view

- Capsule is adherent and consistency is firm.
 - So, the specimen is identified as “Granular contracted kidney” (Figs 4.3A and B).

What are the main causes of granular contracted kidney?

1. Chronic glomerulonephritis: Most common cause.
2. Benign nephrosclerosis
3. Chronic pyelonephritis
4. Less common causes:
 - Terminal stages of:
 - Amyloid/myeloma kidney
 - Diabetic nephropathy.

What are the main causes of chronic glomerulonephritis?



Describe the morphology of chronic GN.

Gross morphology:

- The kidneys are symmetrically contracted.
- They have diffusely granular cortical surfaces.
- On section, the cortex is thinned.
- There is an increase in peripelvic fat.

Histology:

The glomerular histology depends on the stage of the disease.

| Stages | Histology |
|-------------|--|
| Early stage | The glomeruli still show evidence of the primary disease (as given in the causes of the chronic GN above) |
| Late stage | Obliteration of glomeruli transforms the glomeruli into acellular eosinophilic masses, consisting of a combination of: <ol style="list-style-type: none"> 1. Hyaline 2. Collagen 3. Trapped plasma proteins 4. Increased mesangial matrix (Fig. 4.4) |

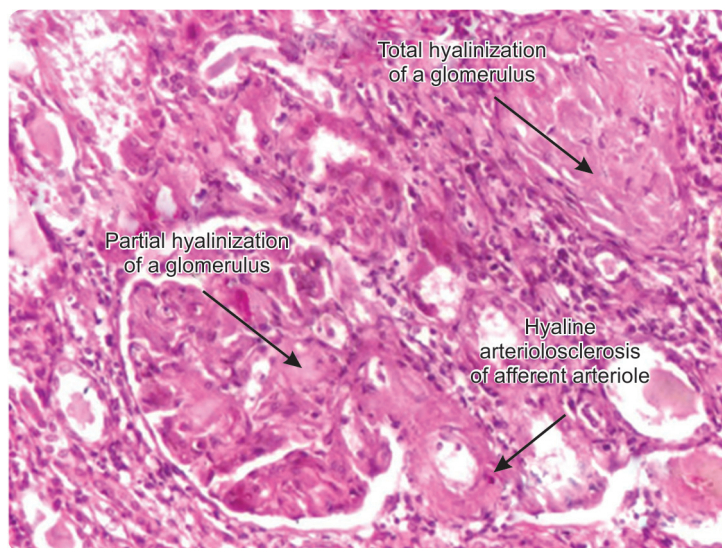


Fig. 4.4: Histology of late stage chronic glomerulonephritis. Reproduced under the permission of Dr Mihai Danciu, Gr T Popa University of Medicine and Pharmacy, Iasi, Romania

What is the association between chronic GN and hypertension?

- Most patients with chronic GN are hypertensive.
- Sometimes the dominant clinical manifestations are cerebral/cardio-vascular.
- Because hypertension is an usual associated condition of chronic glomerulonephritis, the following histological features may be seen:
 1. Hyaline arteriosclerosis (Fig. 4.4)
 2. Marked atrophy of associated tubules.

Describe the important urinary findings in such a case.

What is the treatment of chronic GN?

- There are very few options left as the kidneys are slowly progressing to renal insufficiency and the patients may die of uremia in upcoming years.
- The only options are:
 - a. Continued dialysis
 - b. Renal transplant.
- But in patients with long-term dialysis, certain risks are there like:
 - a. Acquired cystic disease.
 - b. Increased number of renal adenomas and carcinomas.
- So, renal transplant seems to be the only option.

| Parameters | Description |
|---------------|---|
| Physical | <ul style="list-style-type: none">• Volume: Large• Color: Pale• Transparency: Clear• Specific gravity: Low and fixed (1010)— Isothenuria |
| Chemical | Mild to moderate proteinuria |
| Microscopical | Granular cast present |

Hydronephrosis

Description

- The kidney is enlarged.
- Cut section shows multiple cystic cavities which are communicating with renal pelvis.
- Wall of cyst is very thin and devoid of congestion.
- Pelvis of ureter is dilated.
 - So, the specimen is identified as “Hydronephrosis” (Figs 4.5A and B).

Why this is not a specimen of polycystic kidney?

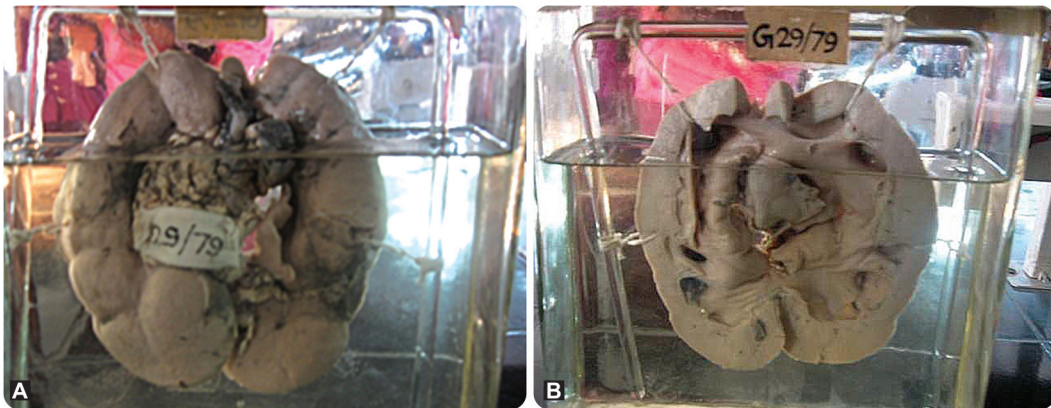
Because in polycystic kidney, the cysts do not communicate with renal pelvis.

Why this is not a specimen of pyelonephritis?

Because in pyelonephritis, the cyst walls are inflamed and congested.

What is hydronephrosis?

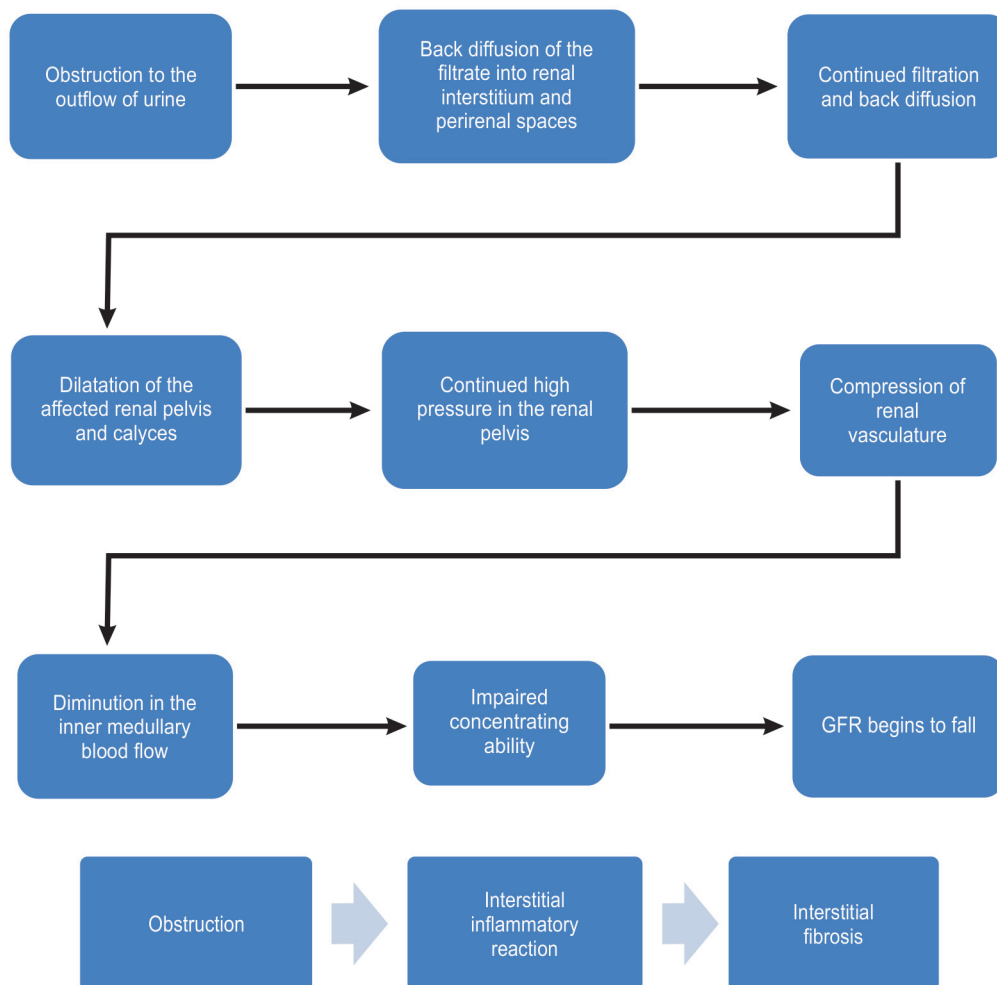
Hydronephrosis is described as dilation of the renal pelvis and calyces associated with progressive atrophy of the kidney due to obstruction to the outflow of urine (Figs 4.6A and B).



Figs 4.5A and B: Hydronephrosis. A. Front view and B. Back view

Name some causes of hydronephrosis.

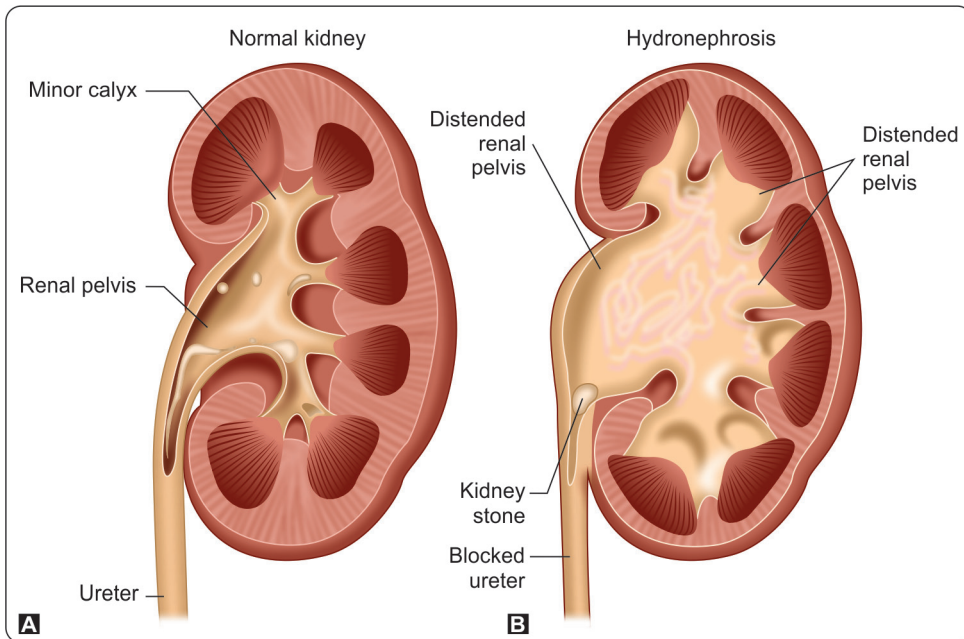
| Locations | Causes |
|-------------------------|--|
| Pelvis | <ul style="list-style-type: none"> • Calculi • Tumors |
| Ureter—Intrinsic causes | <ul style="list-style-type: none"> • Calculi • Tumors • Clot • Sloughed papillae inflammation |
| Ureter—Extrinsic causes | <ul style="list-style-type: none"> • Cervical tumors • Retroperitoneal fibrosis |
| Bladder | <ul style="list-style-type: none"> • Calculi • Tumors • Neurogenic bladder |
| Prostate | <ul style="list-style-type: none"> • Benign nodular hyperplasia of prostate • Prostatic carcinoma • Prostatitis |

Describe the pathogenesis of hydronephrosis.**Describe the morphological changes seen in hydronephrosis.**

- The kidney may be slightly to massively enlarged (depending on the degree and the duration of the obstruction).

Introduction:

| <i>Types of obstruction</i> | <i>Effects on glomerular filtration</i> |
|-----------------------------|--|
| Subtotal or intermittent | <ul style="list-style-type: none"> • Glomerular filtration is not suppressed • Progressive dilation of renal pelvis ensues |
| Sudden and complete | <ul style="list-style-type: none"> • Glomerular filtration is reduced • Mild dilation of the pelvis and calyces • Atrophy of the renal parenchyma |



Figs 4.6A and B: A. Normal kidney and B. Kidney with hydronephrosis. Note the distension of the renal pelvis on the right kidney. In this illustration, the distension is caused by a kidney stone blocking the ureter, causing the urine to back diffuse to the renal pelvis

Morphological changes: Compare with the pathogenesis of hydronephrosis.

| Duration of obstruction | Morphological changes |
|-------------------------|---|
| Acute onset | Dilation of the pelvis and calyces with interstitial inflammation |
| Chronic onset | Cortical tubular atrophy with diffuse interstitial fibrosis |
| Advanced case | The kidney is transformed into a thin-walled cystic structure with: <ul style="list-style-type: none"> • Extensive parenchymal atrophy • Total obliteration of the pyramids • Thinning of the cortex |

Polycystic kidney disease

Description

- The kidney is enlarged.

- Multiple small/large cysts are projecting on the surface in bunch.
- In between the cysts, the kidney tissues are white and atrophied.
- **All the cysts fail to communicate with the renal pelvis.**
- Renal pelvis is usually not dilated.
- When the cysts are cut in section, they show multiple cavities which contain viscid/clear fluid. It may be black due to hemorrhage within the cysts.
 - So, the specimen is identified as “Polycystic kidney disease” (Fig. 4.7).

Name some of the diseases where renal cysts are found.

1. Simple renal cyst
2. Polycystic kidney disease:
 - a. ADPKD (Autosomal dominant polycystic kidney disease).
 - b. ARPKD (Autosomal recessive polycystic kidney disease).

3. Multicystic renal dysplasia
4. Medullary cystic disease
5. Glomerulocystic disease
6. Extraparenchymal renal cyst
7. Dialysis associated cystic disease.

Describe the pathogenesis of polycystic kidney diseases in brief.

1. Adult onset/autosomal dominant polycystic kidney disease (ADPKD):

Normal physiology:

- Each renal tubular epithelial cell contains a single nonmotile primary cilium, which projects into the tubular lumen.



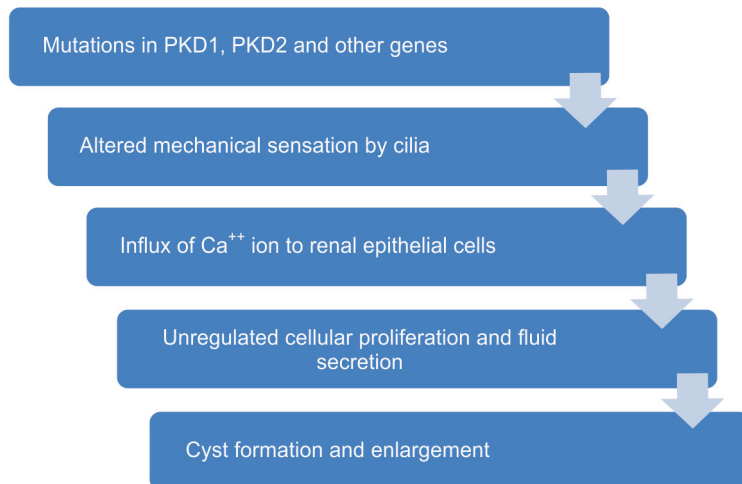
Fig. 4.7: Polycystic kidney disease

- This cilium senses external mechanical signals (e.g.: fluid flow).
- In response to these signals, these cilia regulate Ca^{++} ion flux.
- PKD1 and PKD2 genes translate 2 distinct proteins named polycystin 1 and polycystin 2, which are located in the cilium; possibly regulating the signal transduction (by Ca^{++}) and ultimately, growth and differentiation of tubular epithelial cells.

In ADPKD:

- In ADPKD, either the gene PKD1 or PKD2 is mutated, resulting in mutated polycystin 1/polycystin 2 production.
- So the mechanical sensation and signal transduction mechanism by the cilia are altered; leading to high levels of Ca^{++} influx into the cell and subsequent unregulated growth and differentiation of tubular epithelial cells; eventually leading to cyst development and enlargement of the cyst.

The possible mechanism for cyst formation is:

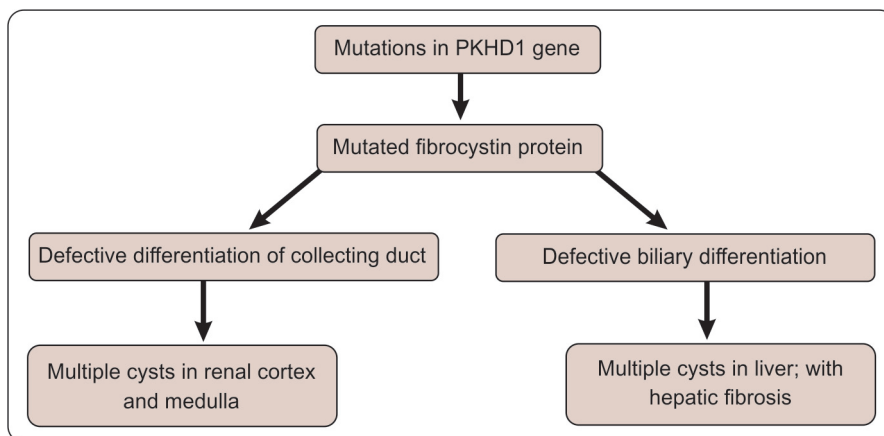


2. Childhood onset/autosomal recessive polycystic kidney disease (ARPKD):

- In most cases, the disease is caused by mutations of the PKHD1 gene which encodes another protein named “Fibrocytin”.
- Fibrocystin is thought to be a cell surface receptor responsible for

differentiation of both collecting duct and biliary tract.

- So mutation in this “Double function” gene leads to the characteristic clinical scenario of:
 - a. Presence of cysts in cortex and medulla
 - b. Presence of cysts in liver, associated with hepatic fibrosis.



Tell some important morphological features of ADPKD and ARPKD.

| Morphological features | ADPKD/Adult PKD | ARPKD/ Childhood PKD |
|-------------------------------|---|--|
| Gross appearance | The kidneys are usually bilaterally enlarged and external surface appears to be composed solely of a mass of cysts, upto 3–4 cm in diameter, with no intervening parenchyma | <ul style="list-style-type: none"> • The kidneys are enlarged and have a smooth external surface • Only a cut section reveals numerous small cysts in the cortex and medulla |
| Prominent microscopic finding | Microscopic examination reveals functioning nephrons dispersed between the cysts | Microscopic examination reveals dilation of all collecting tubules |
| Cell of origin | The cysts arise from the tubules throughout the nephron and therefore have variable lining epithelia | The cysts have a uniform lining of cuboidal cells, reflecting their origin from the collecting ducts |
| Involvement of liver | About 40% of the patients have one to several cysts in the liver (polycystic liver disease) that are usually asymptomatic | In almost all cases the liver has cysts associated with portal fibrosis (congenital hepatic fibrosis). Such patients may develop portal hypertension with splenomegaly |

Name one cystic disease of kidney where most of the cysts are located at the junction of renal cortex and medulla.

Medullary cystic disease.

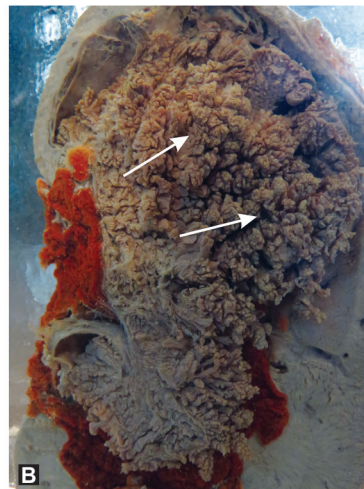
Name one cystic disease of kidney which may progress into renal cell carcinoma (RCC).

Dialysis associated cystic disease.

Renal cell carcinoma

Description

- This is a nephrectomy specimen

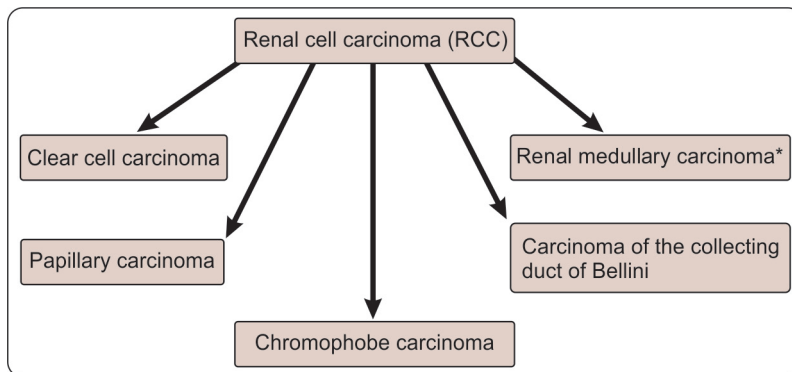


Figs 4.8A and B: A specimen of kidney with renal cell carcinoma showing extensive invasion of renal calyces (arrows) and areas of hemorrhage

showing the cut surface of a kidney with a yellowish orange growth diffusely involving almost the whole of the kidney.

- This growth has extended inside the cut surface and it has invaded the renal calyces.
- Extensive area of hemorrhage and necrosis is being seen.
 - So, this specimen is identified as “Renal cell carcinoma” (Figs 4.8A and B).

What are the major types of renal cell carcinoma?



(*Rare)

Describe the major histological features of some important types of RCC.

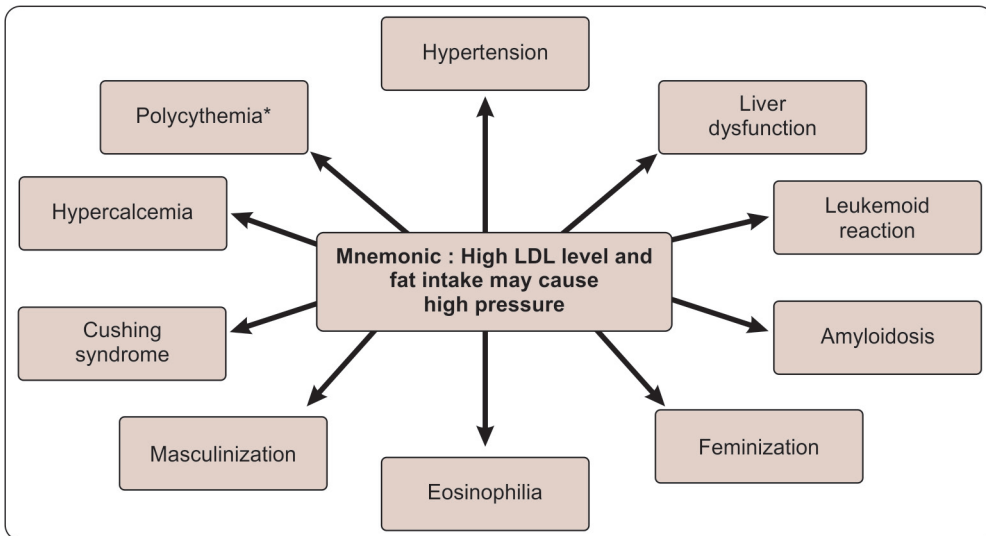
| RCC subtype | Incidence | Development | Growth pattern | Morphology |
|----------------------------|-----------|--|------------------------|--|
| Clear cell | 75% | Solitary, rarely multifocal or bilateral | Solid, tubular, cystic | Clear cytoplasm; cells with eosinophilic cytoplasm occasionally |
| Papillary | 10% | Multifocal, bilateral or solitary | Tubulopapillary, solid | Type 1 (basophilic) or type 2 (eosinophilic) |
| Chromophobe | 5% | Solitary | Solid | Pale or eosinophilic granular cytoplasm, usually with a perinuclear halo |
| Collecting duct of Bellini | 1% | Solitary | Irregular channels | Eosinophilic cytoplasm |

Can you name some genes associated with RCC?

- Clear cell carcinoma is identified by specific deletion of chromosome 3p and mutation of the VHL gene. Other changes are duplication of the chromosome band 5q22, deletion of chromosome 6q, 8p, 9p and 14q.

- Papillary carcinoma is associated most commonly with trisomies of chromosomes 3q, 7, 8, 12, 16, 17 and loss of chromosome Y.

What are the common paraneoplastic syndromes associated with RCC?



(* Polycythemia is the most common paraneoplastic syndrome associated with RCC; it is caused by a high amount of erythropoietin production by the tumor).

What are the classical diagnostic features of RCC?

1. Palpable mass
2. Costovertebral pain
3. Painless hematuria.

Define hematuria.

Hematuria is usually defined as >5 RBCs per high-power field in the urinary sediment.

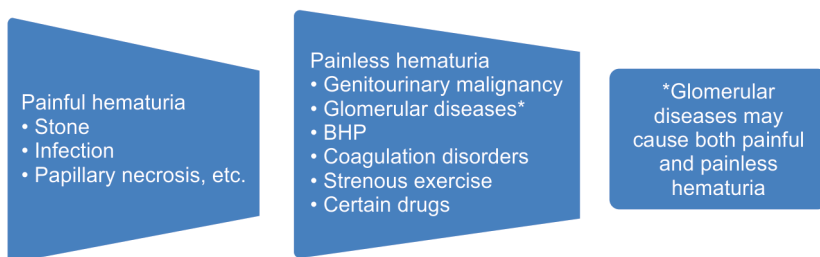
What is the significance of pain associated with hematuria?

hematuria are found to have a malignancy (most commonly bladder cancer).

What are the common metastatic sites for RCC?

It should be mentioned that RCC, being an aggressive tumor, presents with distal metastasis in 1/4th of patients at the time of diagnosis. The common sites for metastasis are:

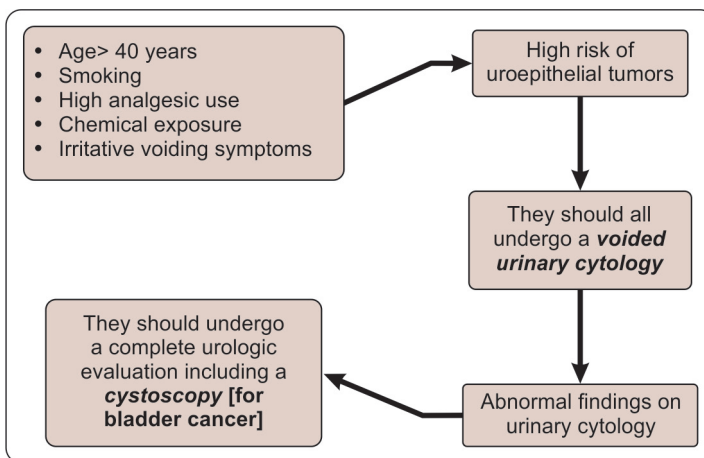
- Lungs and mediastinum



How do you confirm a diagnosis of cancer as a cause of painless hematuria?

30% of the patients with painless

- Bone
- Liver
- Lymph nodes
- Adrenal gland
- Brain.



Male Genital System

CHAPTER

5

Carcinoma penis

Description

It is a specimen of penis with a large cauliflower-like fungating mass having rolled out and everted margin. The surface of growth is ulcerated.



Fig. 5.1: Carcinoma penis. The specimen of penis is showing large cauliflower-like growth at coronal sulcus of the glans penis

- So, the specimen is identified as “Carcinoma penis” (Fig. 5.1).

What are the common sites of origin of carcinoma penis?

In decreased order of frequency

1. Glans penis: Most common
2. Frenulum
3. Prepuce.

What are the common macroscopic types of carcinoma penis?

| Types | Description |
|-----------|---|
| Papillary | Produces cauliflower-like fungating mass |
| Flat | Produces epithelial thickening and eventually progresses into development of an ulcerative lesion |

What is the major histologic type?

Squamous cell carcinoma.

What are the predisposing conditions?

1. Phimosis (when the orifice of the prepuce is too small to permit its normal retraction, the condition is designated as phimosis).

2. Chronic balanitis (Inflammation of the glans penis).
3. HPV type 16 infection.
4. Cigaret smoking.

What is the age of affected people?

Usually between 40 and 70.

What are the premalignant lesions?

1. Bowen's disease
2. Bowenoid papulosis.

What are the modes of spread?

Squamous cell carcinoma of penis is a slow growing and locally invasive carcinoma; disseminated metastasis is extremely uncommon.

Prognosis largely depends on the presence/absence of inguinal lymph node metastasis.

| Mode of spread | Description |
|------------------|---|
| Local spread | <ul style="list-style-type: none"> • Infiltration of erectile tissue |
| Lymphatic spread | <ul style="list-style-type: none"> • In inguinal lymph node • Distal metastasis is uncommon |

Seminoma testis

Description

It is a specimen showing a cut surface of testis which is:

- Homogeneous
- Lobulated
- Gray-white in color
- Devoid of hemorrhage and necrosis.
 - So, the specimen is identified as "Seminoma testis" (Fig. 5.2).

Describe the genetic abnormalities in seminoma testis.

- Seminomas are the most common type of germ cell tumor.
- Seminomas contain an isochromosome 12p.

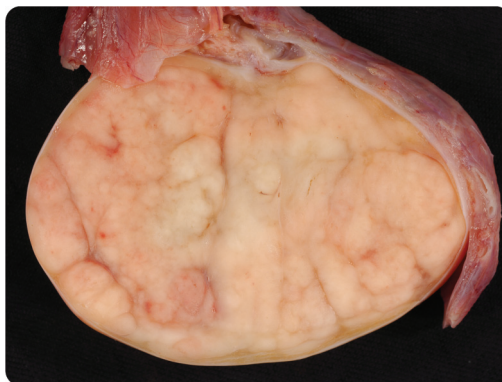
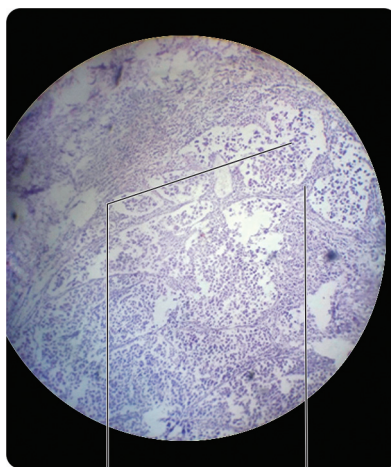


Fig. 5.2: Seminoma testis. A specimen of testis is cut open to show gray-white colored multilobulated tumor. Courtesy of Ed. Uthman, MD, Texas

- Some of the tumors have c-KIT activating mutations.

Describe the morphology of seminoma testis.

- Microscopically the typical seminoma is composed of:
 - Sheets of uniform cells divided into poorly differentiated lobules by



Clusters of tumor cells Fibrous stroma with lymphocytic infiltrate

Fig. 5.3: Testicular seminoma, showing a prominent lymphocytic infiltrate in the fibrous stroma separating the clusters of tumor cells

delicate fibrous septa containing a prominent lymphocytic infiltrate (Fig. 5.3).

- The classic seminoma cell is large and have:
 - A distinct cell membrane.
 - A clear/watery cytoplasm (because of abundant glycogen).
 - A large central nucleus with 1–2 prominent nucleoli.

Benign hypertrophy of prostate/ benign prostatic hyperplasia

Description

It is a specimen of prostate gland showing:

- Enlargement of the gland
- Presence of large, fairly discrete nodules on the periurethral region of prostate.
 - So, the specimen is diagnosed as benign hypertrophy of prostate (Fig. 5.4).

Describe the nodules found in BHP.

- The early nodules are composed almost entirely of *stromal cells*.
- The late nodules are predominantly composed of *epithelial cells*.

Why the diagnosis of BHP can't be made by needle biopsy?

1. Nodules characteristic of BHP usually originates from the **transition zone** of the prostate gland.
2. Needle biopsies cannot typically sample the transition zone.
3. The histology of glandular or mixed



Fig. 5.4: Benign hypertrophy of prostate: Enlargement of both lateral lobes, cut section showing vague nodularity. Capsule intact

glandular-stromal nodules of BHP cannot be appreciated in limited samples.

Describe the pathogenesis of BHP.

Normal physiology:

- There are 2 important types of cells within prostate:
 - A. Stromal cells
 - B. Epithelial cells.
- The activation of testosterone into dihydrotestosterone (DHT) takes place within the stromal cells of prostate by the enzyme type 2 5 α - reductase, which is present only within the stromal cells (not within the epithelial cells).
- After activation, DHT translocates into the nucleus of both epithelial

| Type of nodules | Cell of origin | Morphology | Consistency | Color | Exude fluid? |
|-----------------|------------------|---------------|-------------|-------------|------------------------|
| Early | Stromal cells | Fibromuscular | Tough | Pale-gray | No |
| Late | Epithelial cells | Glandular | Soft | Yellow-pink | Yes; milky white fluid |

cells and stromal cells and attaches to the androgen receptors; then the downstream activity results in growth and differentiation of both types of cells.

In BHP:

Several theories have been proposed to

describe the pathogenesis of BHP. These include:

- An increase in the level of DHT; leading to increased cell growth.
- Reactivation of stem cells in resulting benign enlargement of prostate.
- Unregulated Stromal-epithelial interaction (Fig. 5.5).

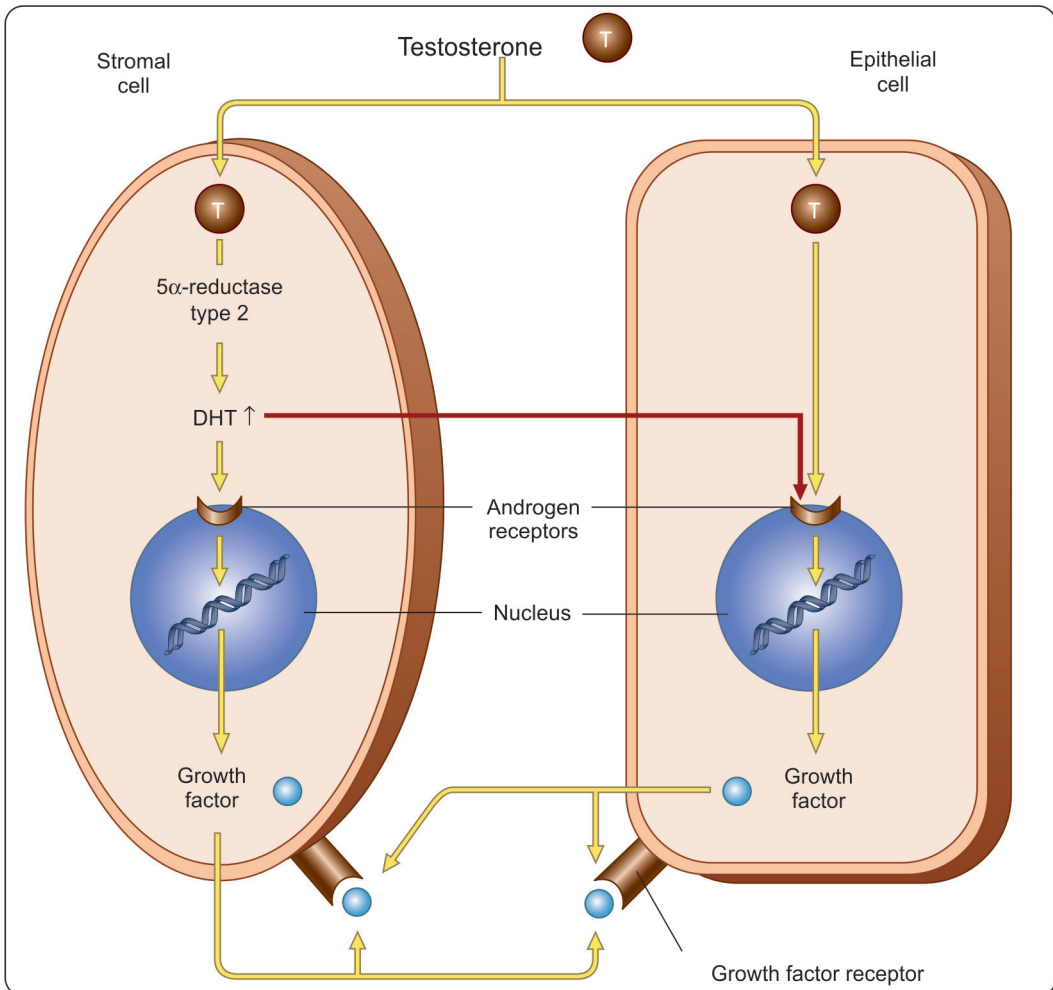
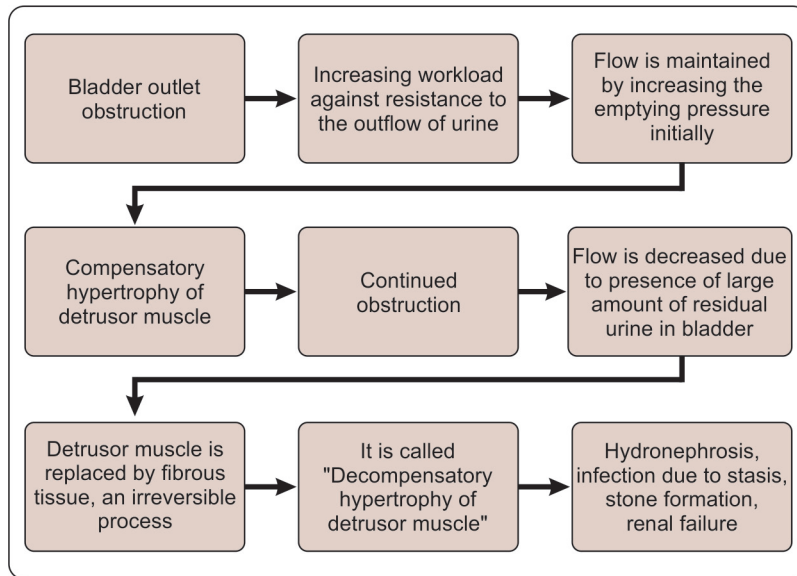


Fig. 5.5: Pathogenesis of BHP

What are the sequelae of BHP?



Can you name some treatment options for BHP?

1. Pharmacological:

- a. Type 2 5α -reductase inhibitor: Finasteride: Interfere with disease progression.

- b. α_1 -adrenergic blocker: Prazosin/ Terazosin/Tamsulosin: Provide symptomatic relief.

2. Surgical: Transurethral resection of prostate (TURP) is gold standard in the term of reduction of symptoms.

CHAPTER

6

Female Genital System

Leiomyoma of uterus

Description

It is a specimen of hemisection of uterus showing irregular nodular growths which are:

- Well-circumscribed
- Whitish in color
- Glistening surface
- Encircled by a fibrous capsule with a typical whorled appearance.

Rest of the uterine muscle looks reddish brown.

- So, the specimen is identified as “Leiomyoma of uterus” (Fig. 6.1).



Fig. 6.1: Leiomyoma of uterus

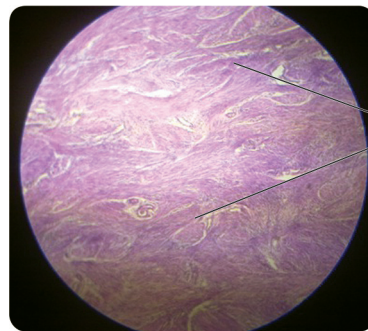
What are the different types of uterine leiomyoma?

According to anatomical location it is classified as:

1. Intramural: Located within the body of uterus.
2. Submucous: When pushed towards uterine cavity.
3. Subserous: When pushed towards peritoneal cavity.

Describe the histology of leiomyoma.

- On microscopy, leiomyoma is composed of whorled bundles of smooth muscle cells that resemble the uninvolved myometrium (Fig. 6.2).



Bundles of smooth muscle

Fig. 6.2: Histology of leiomyoma

- Usually, the individual muscle cells are uniform in size and shape and have the characteristic oval nucleus and long bipolar cytoplasmic processes.

What is the cell of origin of leiomyoma?

Smooth muscle cell.

What is the malignant counterpart of leiomyoma?

Leiomyosarcoma.

What are the sites where leiomyoma are found?

The sites involved are (in decreased frequency):

1. Uterus (most common before the age of 40)
2. Cervix
3. Broad ligament
4. Ovary
5. Retroperitoneum
6. Skin
7. GIT, etc.

Theoretically, it may occur at any site in the body where there is a muscular vessel.

What is the minimum mitotic count for diagnosis of leiomyosarcoma?

10 per 10 high-power fields.

Carcinoma cervix

Description

It is a specimen of cervix and vaginal cuff showing an ulcerated growth with a rolled out margin.

- So, the specimen is identified as “Carcinoma cervix” (Figs 6.3A to C).

What are the different macroscopic types of carcinoma cervix?

1. Fungating type

2. Ulcerative type
3. Infiltrative type.

What are the main histological types of carcinoma cervix?

1. Squamous cell carcinoma (80%)
2. Adenocarcinoma (15%).

What is the causative agent of cervical carcinoma?

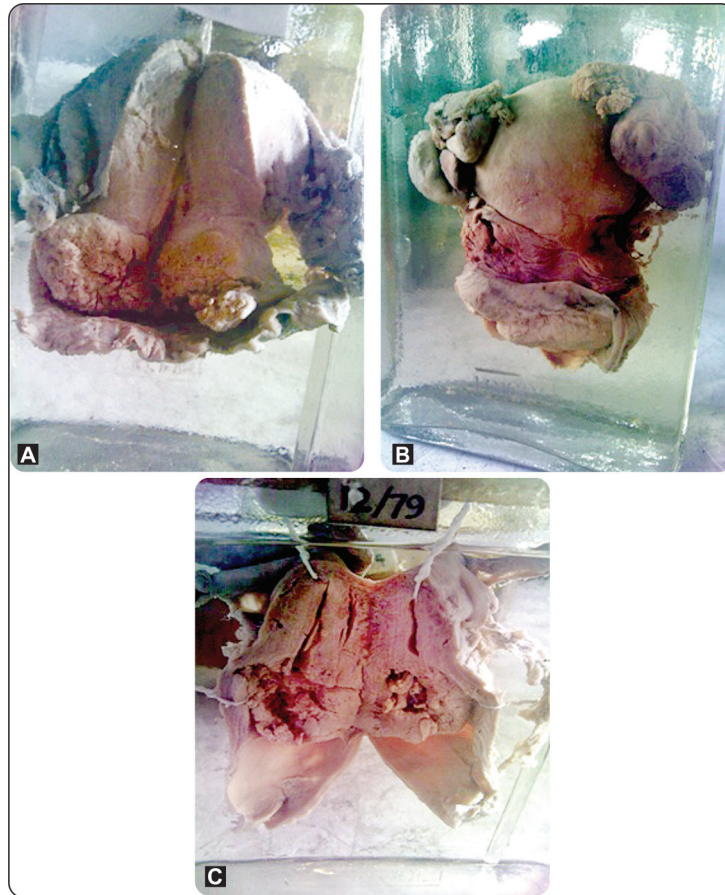
Human papilloma virus (HPV) type 16 and type 18.

What are the important risk factors for carcinoma cervix?

1. Age: Young woman of age: 25–45 years.
2. Past history of genital warts.
3. Marital status: Widowed/divorced/separated/multiple sexual partners.
4. Early marriage/early childbearing/repeated childbirth.
5. Continued use of oral contraceptive pills with high estrogen content.
6. Lower socioeconomic group: With poor genital hygiene.

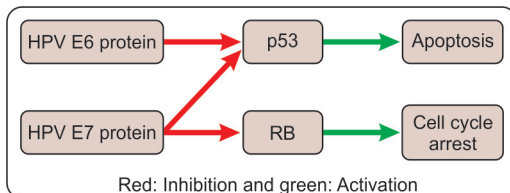
Describe the main points of pathogenesis of cervical carcinoma by HPV.

- HPVs cannot infect the mature superficial squamous cells covering ectocervix/vagina/vulva.
- HPVs can only infect immature basal cells of the squamous epithelium in areas of epithelial breaks present at the squamocolumnar junction.
- The endocervix contains large areas of immature squamous metaplastic epithelium.
- So the endocervix is particularly vulnerable to HPV infection.
- After being integrated with the host genome; the HPV genome produces two viral proteins named E6 and

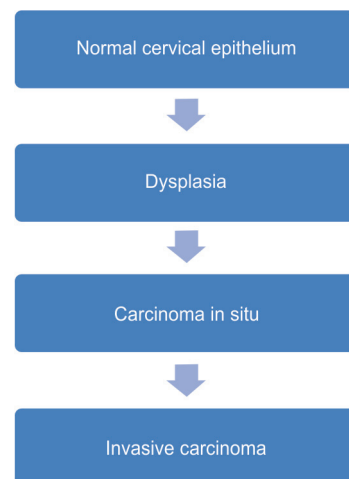


Figs 6.3A to C: Specimens of cervical carcinoma. A and B. Gross, and C. Cut section

E7, which are responsible primarily for the uncontrolled growth and differentiation of immature squamous epithelium of cervix. The mechanism how E6 and E7 work is as follows:



What is the natural course of events in the progression of cancer cervix?



What is the classification system of cervical premalignant lesions?

Three different classification systems had been evolved to describe cervical premalignant lesions. They were based on:

1. Degree of dysplasia
2. Cervical intraepithelial neoplasia (CIN)
3. Squamous intraepithelial lesion (SIL): Most recent classification.

- To understand the approach, all of these 3 systems are being discussed.

| Dysplasia | CIN | SIL |
|-------------------|-------|-------|
| Mild | CIN 1 | LSIL* |
| Moderate | CIN 2 | HSIL |
| Severe | CIN 3 | HSIL |
| Carcinoma in situ | CIN 3 | HSIL |

*LSIL: Low grade SIL; HSIL: High grade SIL.

It should be mentioned that most of the LSIL does not progress to HSIL; but they eventually regress; so **LSIL is not regarded as a premalignant lesion.**

What do you mean by “Koilocytic atypia”? What is its importance?

- **Koilocyte:** It is defined as a squamous epithelial cell that has gone certain structural changes as a result of HPV infection.
- **Koilocytic atypia:** It is a cytopathic effect seen when HPV infects a squamous epithelial cell. It is characterized by:
 - Enlargement of the nucleus
 - Hyperchromasia (dark staining) of the nucleus
 - Irregular nuclear membrane
 - A clear area around the nucleus (Perinuclear halo) (Fig. 6.4).

Importance: The identification of “koilocytic atypia” in cervical microscopy is diagnostic of a dysplastic change within the cells. Now to classify the lesion into LSIL or HSIL, degree of epithelial thickness involvement is measured.

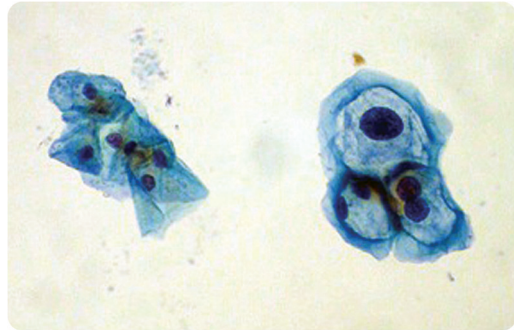


Fig. 6.4: Pap smear with groups of normal cervical cells on the left and HPV infected cells on the right; showing typical koilocytic changes:

- Enlarged nucleus
- Hyperchromasia
- Perineuclear halo.

(Courtesy of Dr Ed Uthman, MD)

How will you diagnose a cervical lesion as LSIL or HSIL?

| Degree of SIL | Characteristic feature towards diagnosis |
|---------------|---|
| LSIL | The dysplastic immature squamous epithelial cells are confined to the lower 1/3rd of the total epithelial thickness |
| HSIL | The dysplastic immature squamous epithelial cells extend greater than lower 2/3rd of the total epithelial thickness |

Name a marker that can detect dysplastic cervical epithelium.

Ki-67 (a marker of cellular proliferation).

How cervical carcinoma is staged?

| Stages | Description |
|---------|---|
| Stage 0 | Carcinoma in situ (CIN III, HSIL); i.e. carcinoma is confined only to the surface layer of cervix |
| Stage 1 | Carcinoma confined to the cervix |
| Stage 2 | Carcinoma extends beyond the cervix but not to the pelvic wall. Carcinoma involves the vagina but not the lower-third |

Contd...

Contd...

| Stages | Description |
|---------|--|
| Stage 3 | Carcinoma has extended to the pelvic wall. The tumor involves the lower-third of the vagina |
| Stage 4 | Carcinoma has extended beyond the true pelvis or has involved the mucosa of the bladder or rectum, also including metastatic dissemination |

Name one test that is used for screening of carcinoma cervix?

1. Pap smear
2. Visual inspection with 5% acetic acid (VIA)
3. VIA with magnification (VIAM)
4. Visual inspection after application of Lugol's iodine (VILI).

What is the definitive treatment of carcinoma cervix?

Radical surgery and radiotherapy.

Dermoid cyst/benign cystic teratoma

Description

This is a specimen of enlarged ovary cut

open to show a unilocular cyst (cyst having a single sac) containing sebum and hair follicles. It may also contain teeth or bone.

- So, the specimen is identified as “Benign cystic teratoma of ovary/dermoid cyst” (Fig. 6.5).

What is a teratoma?

- Teratoma is an encapsulated tumor composed of tissues/organs which are foreign to the part in which it arises.
- It usually develops from all the 3 primitive germinal layers: Ectoderm, mesoderm and endoderm.

What is its origin?

Teratomas belong to a class called “Nonseminomatous germ cell tumors (NSGCT)”. The tumors in the NSGCT group arise from 2 origins: Germ cells and embryonal cells. Teratomas are of germ cell origin.

What are the different sites where teratoma is found?

1. Gonads (the most common site)
2. Sacrococcygeal region
3. Retroperitoneum
4. Mediastinum

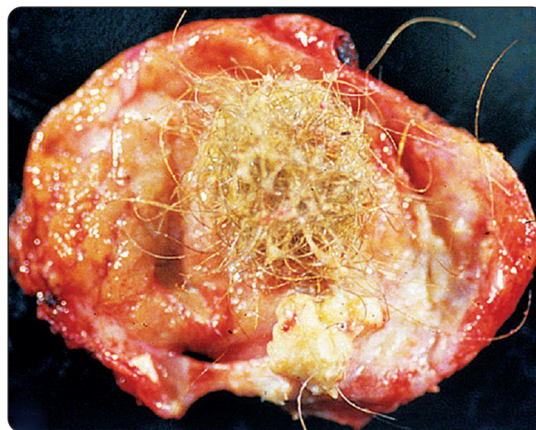


Fig. 6.5: Dermoid cyst/ Benign cystic teratoma. The cyst cavity is filled with a thick, greasy fluid and often contains cartilage, hair and well-formed teeth. Reproduced under the permission of “Health, Medicine and Anatomy Reference Pictures” (www.healthfavo.com)

5. Nasopharynx
6. Base of the skull, etc.

What are the different types of teratoma?

Teratoma is usually of 3 types:

1. Mature teratoma/benign cystic teratoma/dermoid cyst.
2. Immature teratoma/malignant teratoma.
3. Monodermal/specialized teratoma.

What are the characteristic features of a dermoid cyst?

1. Dermoid cyst usually contains hair and adnexal structures of the skin and other structures; which are derived from ectoderm (Fig. 6.6).
2. **As it contains only mature tissue, a dermoid cyst is benign as a rule.**
3. The wall of dermoid cyst is formed by stratified squamous epithelial cells, which very rarely may develop into squamous cell carcinoma in adults.
4. Infrequently, a dermoid cyst may

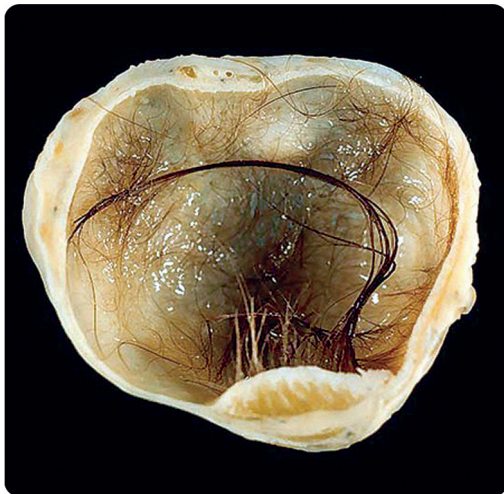


Fig. 6.6: Benign cystic teratoma of ovary showing abundant hair and other cutaneous structures. (Courtesy of Dr Ed Uthman, MD)

contain tissues derived from all the 3 germ cell layers (Fig. 6.7).

Describe the morphology of benign cystic teratoma.

- On histologic examination the cyst wall is composed of stratified squamous epithelium with:
 - a. Sebaceous glands
 - b. Hair shafts
 - c. Skin, etc.
- In some cases structures from other germ layers can be identified, such as:
 - a. Cartilage
 - b. Bone
 - c. Thyroid tissue
 - d. Neural tissues.

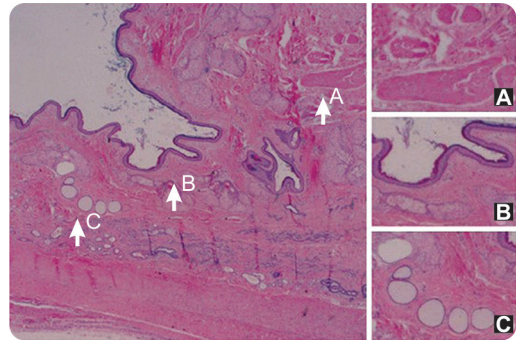


Fig. 6.7: Histology of a benign mature teratoma. A. Muscle, B. Skin and skin appendage, C. Mucous cyst. Reproduced under the permission of Korean Endocrine Journal and Dr Byung Joon Kim, Division of Endocrinology and Metabolism, Department of Internal Medicine, Konyang University College of Medicine, Korea

What are the complications of benign cystic teratoma?

1. Torsion of the cyst.
2. Rupture of the cyst with severe foreign body reaction in peritoneum.
3. Malignant transformation (in 1% of cases).

CHAPTER

7

Breast

Breast carcinoma

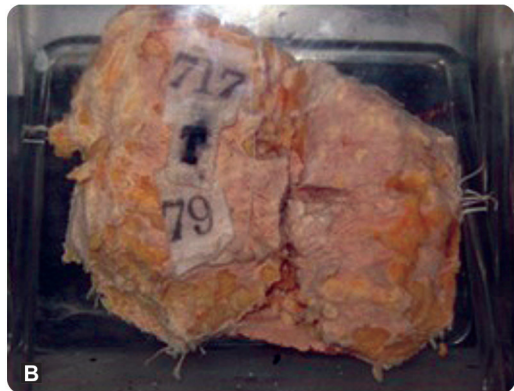
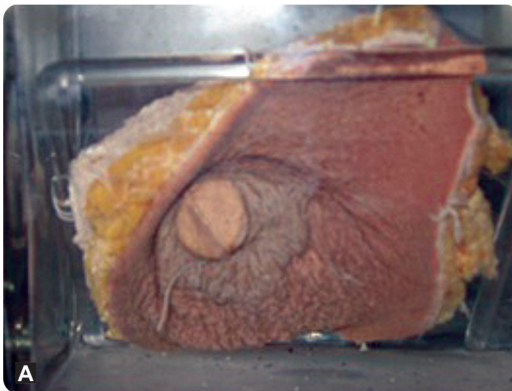
Description

- It is a specimen showing hemisection of breast with a grayish yellow growth.
- The growth is irregular in shape with poorly defined margins extending into the surrounding tissue.
- Nipple is retracted and skin on surface presents an orange peel like dimpled structure.
 - So, the specimen is identified as “Carcinoma breast” (Figs 7.1A and B).

(The growth, if felt, is hard and if cut, grating sound is heard).

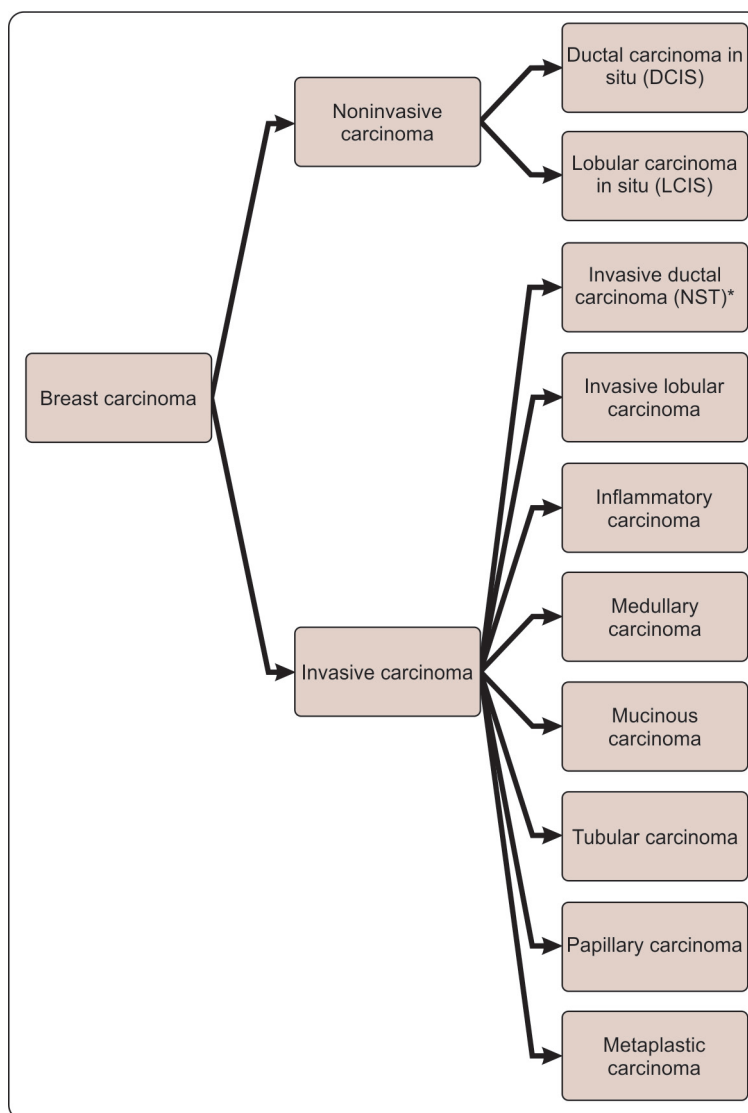
Name some of the common genes which are mutated in breast carcinoma?

- BRCA1
 - BRCA2
 - CHEK2
 - p53.
- Mutations in these genes are associated with hereditary breast cancer.



Figs 7.1A and B: Breast carcinoma

How will you classify carcinoma breast?



(*NST: No special type)

What are the proposed cells of origin of breast carcinoma?

- ER+ve breast carcinoma: Luminal cells.
- ER-ve breast carcinoma: Myoepithelial cells.

How will you diagnose a case of breast carcinoma?/ What is triple assessment?

If any patient presents with a breast lump/ other symptoms suspicious of carcinoma, the diagnosis should be made by a combination of:

1. Clinical assessment
2. Radiological study

3. Pathological examination with tissue sample.
 - It is called triple assessment.
- Triple assessment—
1. **Clinical assessment:**
 - a. Age of the patient
 - b. Clinical examination.
2. **Radiological study:**
 - a. Mammography
 - b. Ultrasound scan.
3. **Pathological examination:**
 - a. FNAC: Fine needle aspiration cytology
 - b. Breast core biopsy.

Which type of breast carcinoma has worst prognosis?

Inflammatory carcinoma.

Which type of breast carcinoma has most favorable prognosis?

Noninvasive carcinoma. Particularly LCIS.

What are the histological subtypes of DCIS?

1. Comedocarcinoma
2. Solid
3. Cribriform
4. Papillary
5. Micropapillary.

What are the gene expression profiles of various types of invasive ductal carcinoma/ NST?

| Type of invasive ductal carcinoma | ER (Estrogen receptor) | PR (Progesterone receptor) | HER2/neu | Comment |
|-----------------------------------|---------------------------|-------------------------------|----------|--|
| Luminal A | + | + | – | Most common invasive ductal carcinoma |
| Luminal B | + | + | + | Triple positive phenotype |
| Basal-like | – | – | – | Triple negative phenotype |
| Normal breast-like | + | + | – | Morphology similar to normal breast tissue |
| HER2 positive | – | – | + | Treated with Herceptin (monoclonal antibody against HER2/ neu) |

What are the different modes of metastasis of breast carcinoma?

| Route of spread | Site of metastasis |
|---------------------|---|
| Lymphatic | <ul style="list-style-type: none"> • Axillary lymph node • Internal mammary node • Mediastinal lymph node • Supraclavicular lymph node • Lymphatic spread may extend to the contralateral breast |
| Hematogenous | <ul style="list-style-type: none"> • Lung • Liver • Bones • Adrenal • Brain • Ovary |
| Transcelomic spread | Spread to ovary forming Krukenberg's tumor |

How will you stage breast cancer?

| Stages | Subdivision | Extent [T] | Positive lymph nodes [N] | Metastasis [M] |
|--------|-------------|---|--------------------------|----------------|
| 0 | | DCIS/ LCIS | 0 | – |
| 1 | | Invasive CA \leq 2cm | 0 | – |
| 2 | 2A | Invasive CA $>$ 2 cm | 0 | – |
| | 2B | Invasive CA $<$ 5 cm | 1–3 | – |
| 3 | 3A | Invasive CA $>$ 5 cm | 1–3 | – |
| | 3B | Any size invasive CA | \geq 4 | – |
| | 3C | Invasive CA with skin or chest wall involvement or inflammatory carcinoma | –Ve/ +Ve | – |
| 4 | | Any size invasive CA | –Ve/ +Ve | + |

Give the name of one benign, one intermediate and one malignant tumors of breast.

1. Benign: Fibroadenoma
2. Intermediate: Phyllodes tumor
3. Malignant: Invasive ductal carcinoma.

CHAPTER

8

Bones and Joints

Sequestrum

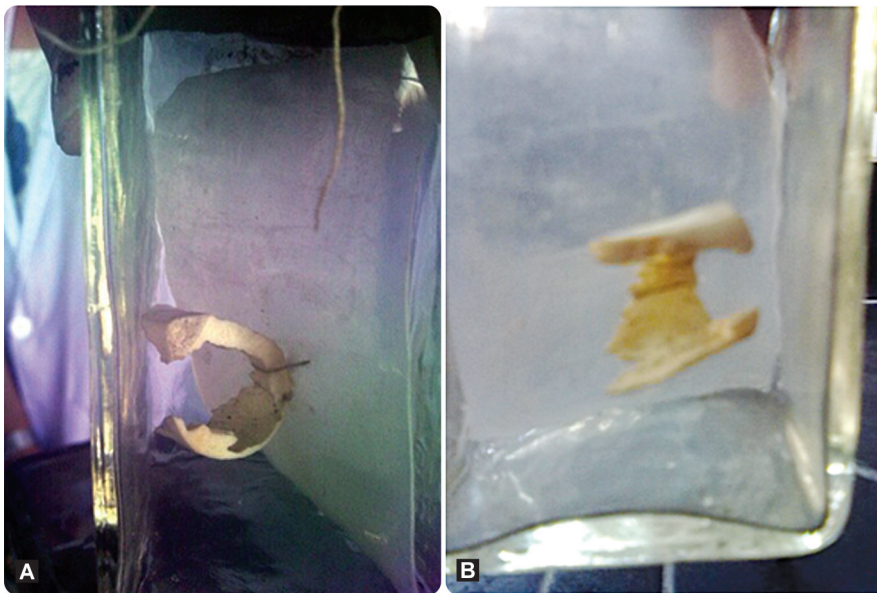
Description

It is a specimen of white, dry, irregular ring-shaped piece of bone with granular surface.

- So, this is a specimen of “Ring sequestrum” (Figs 8.1A and B).

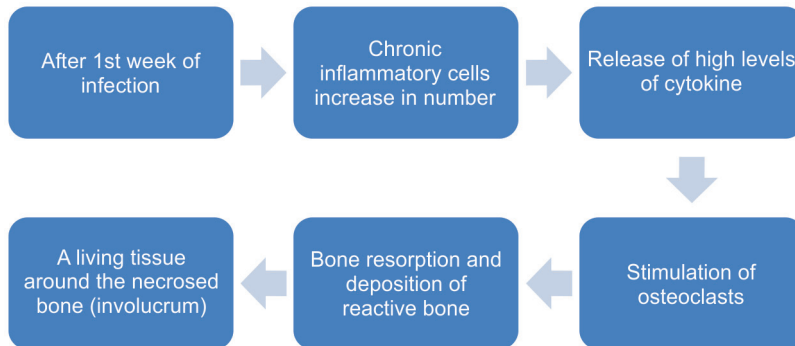
What is a sequestrum?

It is a piece of necrosed bone which gets separated from living tissue in case of chronic osteomyelitis.



Figs 8.1A and B: Sequestrum

What is involucrum?



- After the above sequence of events in chronic osteomyelitis, when the newly deposited bone forms a piece of living tissue around the segment of devitalized infected bone, it is known as an involucrum.

What are the main causative agents of pyogenic osteomyelitis?

1. *Staphylococcus aureus* (80–90% of cases: more common in intravenous drug abusers).
2. *Escherichia coli*, *Pseudomonas*, and *Klebsiella* (individuals with genitourinary tract infections).
3. Mixed bacterial infections (inoculation of organisms during surgery or open fractures).
4. *Haemophilus influenzae* (neonatal period).
5. *Salmonella* (sickle cell disease).
6. In almost 50% of cases, no organisms can be isolated.

What is the most common organism responsible for osteomyelitis?

Staphylococcus aureus.

How the organisms lodge into the bone and where?

- Metaphysis of long bone is a highly vascularized zone, where the medullary arteries and medullary veins branch into capillaries in a specific pattern called “Hairpin arrangement” (Fig. 8.2).
- The blood stasis resulting from such an arrangement is responsible for the metaphysis being a favorable site for bacteria to settle.
- So the organisms pass through the bone, get lodged in the metaphysis.
- Lower femoral metaphysis is the most common site.

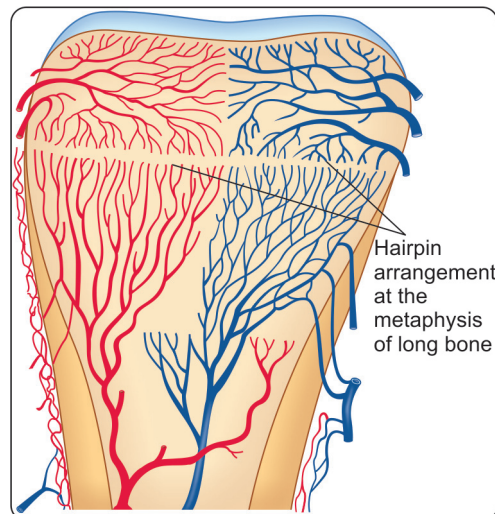
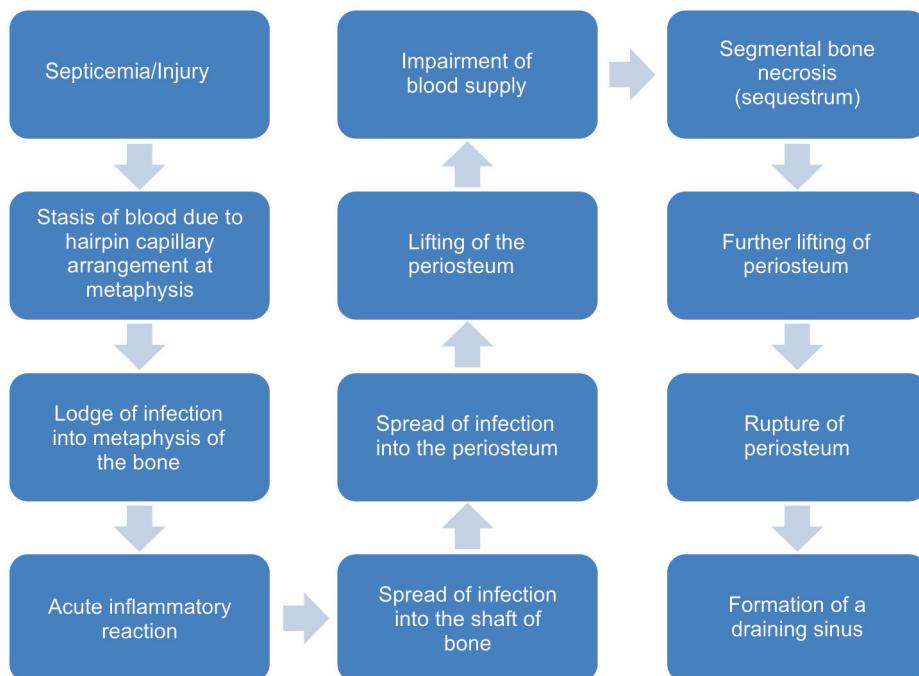


Fig. 8.2: Hairpin arrangement of medullary veins and arteries

How will you diagnose a case of acute and chronic osteomyelitis?

| Parameters | Acute osteomyelitis | Chronic osteomyelitis |
|----------------------|--|--|
| Presenting complaint | Acute onset of pain and swelling at the end of a bone, associated with systemic features of infection like fever | A chronic discharging sinus is the most common presenting complaint. They may heal for short periods; only to reappear with each acute exacerbation |
| Examination findings | The patient is febrile and dehydrated with classical signs of inflammation: redness/heat, etc. localized to the metaphysis of the bone | A chronic discharging sinus with a thickened bone and mild tenderness on deep palpation; adjacent joint may be stiff due to extensive scarring of soft tissues |
| Blood | PMN (polymorphonuclear) leukocytosis with an elevated ESR | Normal |
| X-ray | Periosteal new bone deposition at the metaphysis | <ul style="list-style-type: none"> – Thickening of cortex – Focal areas of sclerosis – Sequestrum (dead piece of bone) surrounded by granulation tissue – Involucrum (dense sclerotic lesion overlying the sequestrum) may be seen |

Describe the pathogenesis of pyogenic osteomyelitis in short.

- After the first week the number of chronic inflammatory cells increases and their release of cytokines stimulate osteoclastic bone resorption and at the same time, deposition of reactive bone in the periphery.
- When the newly deposited bone forms a piece of living tissue around the necrosed bone segment, it is known as an involucrum.

What are the complications of acute and chronic osteomyelitis?

| <i>Complications of acute osteomyelitis</i> | <i>Complications of chronic osteomyelitis</i> |
|---|--|
| Chronic osteomyelitis (most commonly due to a delay in diagnosis) | Episodes of acute exacerbation (due to reactivation of infection) |
| Acute pyogenic arthritis (occurs in case of an intra-articular joint, e.g. hip) | Growth abnormalities: <ul style="list-style-type: none"> • Shortening • Lengthening • Deformities |
| Pathological fractures | Pathological fractures |
| Growth plate disturbances | Joint stiffness |
| Sinus tract malignancy | Amyloidosis |

Tuberculosis of spine (Pott's disease)

Description

This is a specimen of hemisection of a spine showing destruction of a part of vertebra and intervertebral disc.

- So, the specimen is identified as “Tuberculosis of spine/Pott's disease” (Figs 8.3A and B).

Why this is not a metastatic lesion?

This is not a metastatic lesion because in the metastatic lesion, intervertebral discs are not affected.

Which are the most common sites of involvement of tuberculous osteomyelitis?

1. Spine (especially lumbar and thoracic vertebrae)
2. Knee
3. Hip.

What is the incidence of a pulmonary TB patient to have an osseous infection?

1–3 %.

Why “Night crying” is characteristic of Pott's disease?

1. The affected portions of spine are supported while awake (in the day time) by muscular spasm.
2. But in the time of sleeping (at night), muscles relax which allows painful movements to take place. This intense pain is responsible for the night cries in children.

What are the complications of TB spine?

1. Severe destruction of vertebrae → Permanent compression fractures → Deformities (scoliosis/ kyphosis)
2. Compression of the spinal cord → Neurologic deficits
3. Tuberculous arthritis
4. Sinus tract formation
5. Psoas abscess
6. Amyloidosis.

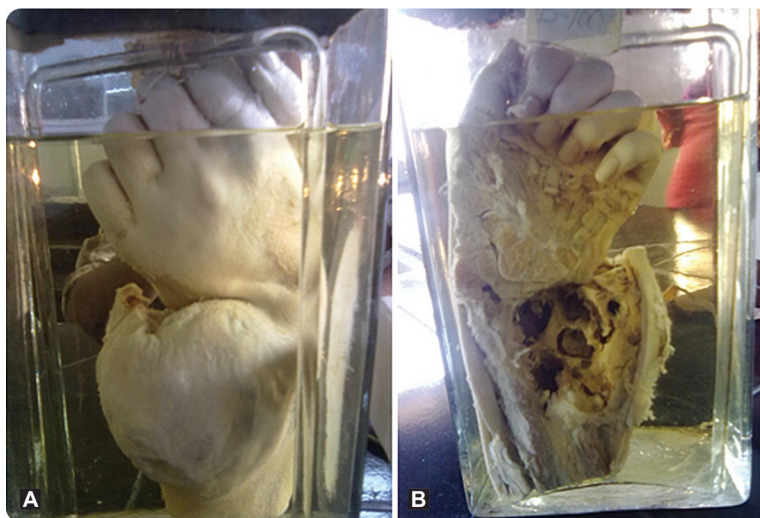


Figs 8.3A and B: Tuberculosis of spine. A. Front view and B. Back view

Giant cell tumor of bone

Description

- It is a specimen showing a fusiform growth at the end of ulna.
- The growth has expanded from inner portion of the bone, pressing the cortical bone into a thin shell at the surface of the growth.
- Cut surface is dark tan in color.
- Blackish areas of hemorrhage, necrosis and cystic change are being seen.
 - So, the specimen is identified as “Giant cell tumor of bone/osteoclastoma” (Figs 8.4A and B).



Figs 8.4A and B: Giant cell tumors (GCT) of bone

What is the most common site of a GCT bone?

Around the knee joint. (Then comes the distal radius and sacrum).

Which part of the bone is commonly affected?

- **Adult:** Metaphysis and epiphysis.
- **Adolescent:** Metaphysis.

What is the behavior of giant cell tumor of bone?

GCT of bone is a benign but locally aggressive tumor.

Describe the morphological features of a GCT.

- The tumor stroma is highly vascular.
- They are mostly composed of uniform oval mononuclear cells that represent the proliferating component of the tumor.
- There are numerous osteoclast-type giant cells having ≥ 100 nuclei scattered within this background; giving the name "Osteoclastoma" (Fig. 8.5).

- Necrosis and hemorrhage are commonly seen.

What is the cell of origin of GCT?

GCT bone is thought to be of mesenchymal origin.

What are the criteria of malignancy in a GCT of bone?

1. Pleomorphism
2. Increased mitosis of stromal cells
3. Reduction in the number and size of giant cells.

How will you diagnose a case of GCT?

Confirmation of the diagnosis: We will take an anteroposterior view and a lateral view X-ray of the affected joint. The following characteristic features will help us differentiating it from other solitary lytic lesions of the bone.

Positive points:

- A. Occurs only with a closed growth plate.
- B. Eccentric location of the tumor.
- C. Well-defined with nonsclerotic margins.

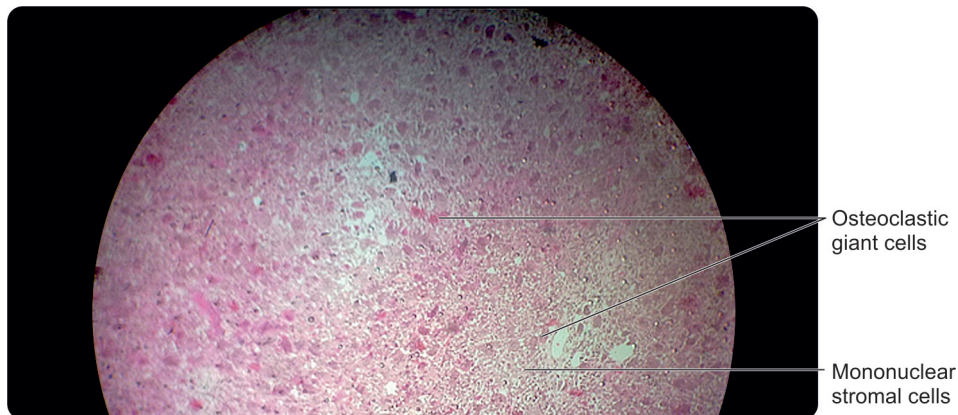


Fig. 8.5: Light microscopy of giant cell tumor illustrating an abundance of multinucleated giant cells with a background of mononuclear stromal cells

- D. The characteristic “Soap bubble appearance”, i.e. the trabeculae of the remaining bone traversing the tumor, giving the tumor a “Sac-like appearance” (Fig. 8.6).



Fig. 8.6: GCT of distal radius

Note: The subarticular location, expansile nature and characteristic “Soap bubble appearance.” (Reproduced under the permission of Dr Wael Nemattalla, Radiopaedia.org)

Negative points:

- A. No calcification and no new bone formation within the tumor.
- B. The tumor usually does not invade the adjacent joint(s).

Name some of the common bone lesions which contain osteoclastic giant cells.

1. Giant cell tumor of bone
2. Simple bone cyst
3. Aneurysmal bone cyst
4. Chondromyxoid fibroma
5. Benign chondroblastoma
6. Brown tumor of hyperparathyroidism.

Osteosarcoma

Description

- It is a specimen of a long bone showing bulky gray-white growth at the end of the bone.
- Cut surface is grayish white with areas of hemorrhage and necrosis.
- The bone cortex is destroyed.
 - So, the specimen is identified as “Osteosarcoma” (Fig. 8.7).



Fig. 8.7: Osteosarcoma

What is the cell of origin?

Primitive mesenchymal cell.

What are the types of osteosarcoma?

There are two types of osteosarcoma:

1. **Primary osteosarcoma:**
 - I. It is usually seen in 15–25 years of age group.
 - II. It occurs without any past history of known premalignant conditions of bone but it is much more malignant than the secondary osteosarcoma.

2. **Secondary osteosarcoma:**

- I. It is usually seen in >45 years of age.
- II. It occurs with a past history of known premalignant conditions of bone (like Paget's disease, fibrous dysplasia of bone, irradiation to bones, multiple osteochondroma, etc.).

What are the different histological types of osteosarcoma?

- A. **Osteoblastic type:** With extensive new bone formation.
- B. **Chondroid type:** With basic cell being a cartilage cell.
- C. **Fibroblastic type:** With basic cell being a fibroblast.
- D. **Osteolytic type:** A predominantly lytic tumor.

What are the bones/joints commonly involved in osteosarcoma?

1. Knee joint (most common)
2. Hip joint
3. Shoulder joint.

What is the most common type of osteosarcoma?

The most common subtype arises in the metaphysis of long bones and is primary, solitary, intramedullary, and poorly differentiated in nature.

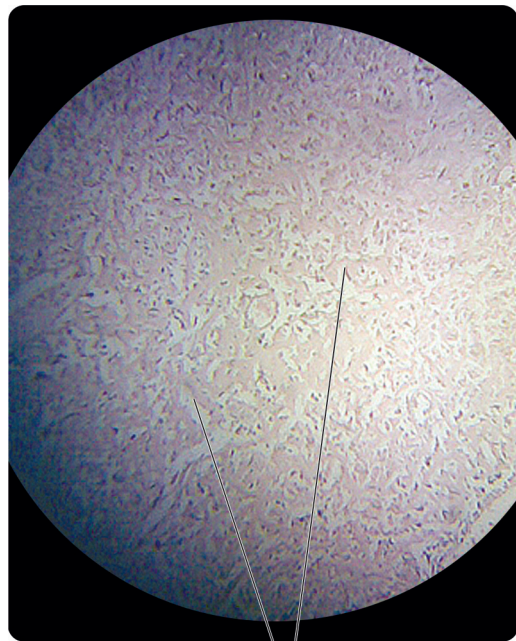
Describe the invasion of long bones by osteosarcoma.

- They spread extensively in the medullary canal, infiltrating and replacing the marrow.
- When joint invasion occurs, the tumor grows into it in either of the 2 ways:
 1. Along the muscle tendons
 2. Along the attachment site of the joint capsule.
- The tumors frequently destroy the

surrounding cortices and produce soft tissue abscesses.

Describe the morphology of osteosarcoma.

- The formation of bone by the tumor cells is characteristic of osteosarcoma.
- The neoplastic bone forms in a characteristic dense, lace-like pattern (Fig. 8.8).
- The tumor cells frequently have large hyperchromatic nuclei.
- Tumor giant cells are commonly seen.



Characteristic lace-like pattern of new bone formation

Fig. 8.8: Morphology of osteosarcoma

Is the tumor aggressive? If yes, how will you detect its aggressiveness?

Yes, the tumor appears to be aggressive, metastasizing frequently all over the body, at first to the lung.

To detect the aggressiveness/metastasis of the tumor, a SAP (serum alkaline phosphates test) has to be done.

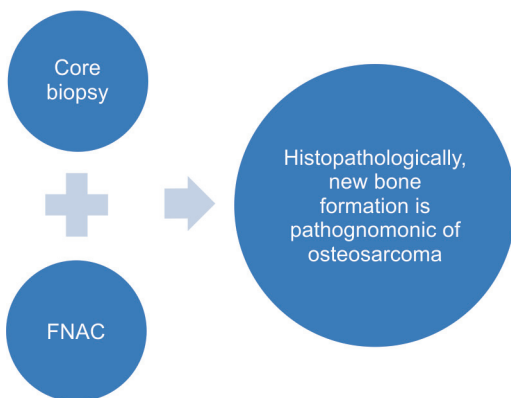
Although it is a nonspecific test, but a *higher value after initial lowering* after tumor excision indicates new metastasis of residual tumor/recurrence.

How will you confirm a diagnosis of osteosarcoma?

A. X-ray:

- I. An area of irregular destruction of metaphysis.
- II. The cortex is eroded.
- III. There is new bone formation in the matrix of the tumor, which lifts the periosteum.
- IV. A triangular area of subperiosteal new bone is seen in the tumor-cortex junction; known as “Codman’s triangle” (Fig. 8.9).
- V. New bone is laid down along the blood vessels growing centrifugally within the tumor; responsible for a “Sunray appearance”.

B. Open biopsy:



What is Codman’s triangle? Name some cases where it is seen.

It is a triangular area of new subperiosteal bone formation usually formed when a tumor/lesion of the bone lifts the periosteum away from the bone.

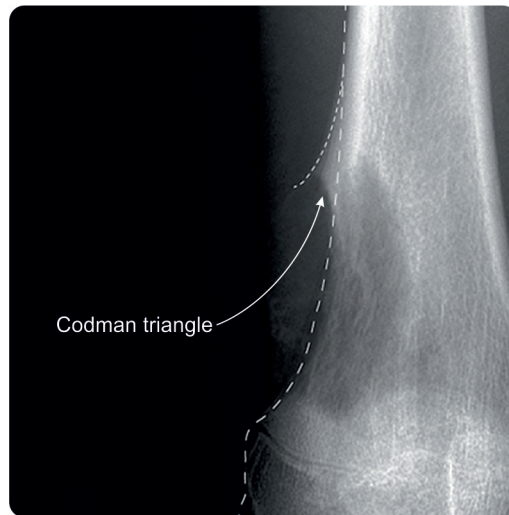


Fig. 8.9: Codman’s triangle. Courtesy of Dr frask Gaillard and Radiopaedia.org.

Main causes for Codman’s triangle:

- Osteosarcoma
- Ewing’s sarcoma
- Subperiosteal abscess.

Name some other osteoblastic tumors of bone.

1. Osteoma
2. Osteoid sarcoma
3. Osteoblastoma
4. Osteochondroma.

CHAPTER

9

Respiratory System

At first we will recapitulate the basic gross anatomy of lung (Fig. 9.1).

Lobar pneumonia of lung

Description

- The specimen is a cut section of lung showing solidification of a lobe.
- The area of solidification looks solid and yellowish gray in color.
 - So, the specimen is identified as “Lobar pneumonia of lung” (Fig. 9.2).

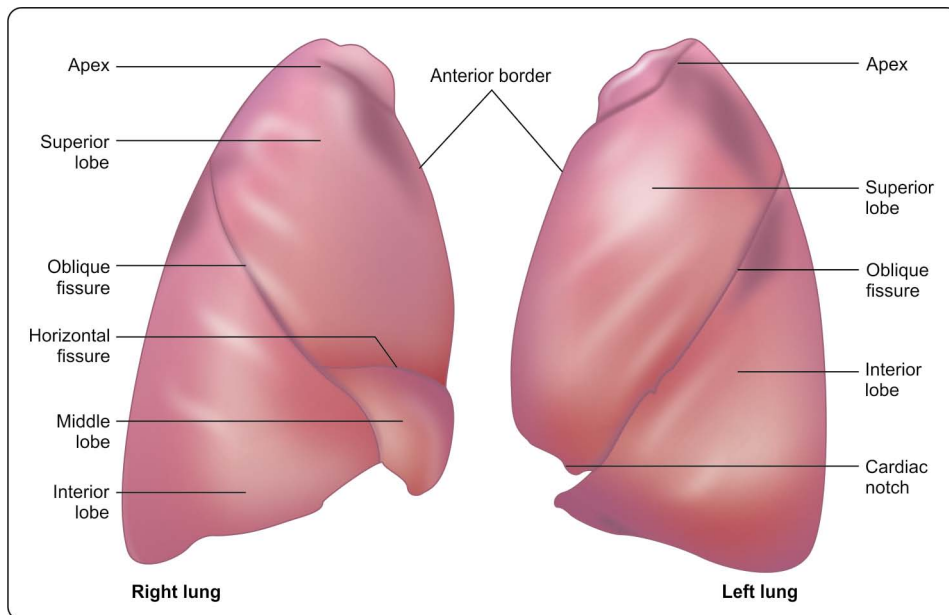


Fig. 9.1: Basic anatomy of lung



Fig. 9.2: Lobar pneumonia of lung. Cut surface of lung showing gray-white consolidated areas, dry, granular in appearance with liver like consistency

What are the causative agents of lobar pneumonia of lung?

| Types of pneumonia | Causative agents |
|---------------------------------------|--|
| Community-acquired acute pneumonia | <ol style="list-style-type: none"> 1. <i>Streptococcus pneumoniae</i> 2. <i>Haemophilus influenzae</i> 3. <i>Moraxella catarrhalis</i> 4. <i>Staphylococcus aureus</i> 5. <i>Legionella pneumophila</i> 6. <i>Klebsiella pneumoniae</i> 7. <i>Pseudomonas</i> spp |
| Community-acquired atypical pneumonia | <ol style="list-style-type: none"> 1. <i>Mycoplasma pneumoniae</i> 2. Chlamydia spp. (<i>C. pneumoniae</i>, <i>C. psittaci</i>, <i>C. trachomatis</i>) 3. <i>Coxiella burnetii</i> (Q fever) 4. Viruses: <ol style="list-style-type: none"> A. Influenza A and B (adults) B. Parainfluenza virus (children) C. Adenovirus D. Respiratory syncytial virus E. SARS virus |
| Hospital-acquired pneumonia | <ol style="list-style-type: none"> 1. <i>Klebsiella pneumoniae</i> 2. <i>Escherichia coli</i> 3. <i>Pseudomonas</i> spp 4. <i>Staphylococcus aureus</i> (usually penicillin resistant) |

What is meant by consolidation?

Replacement of alveolar air by inflammatory infiltrates.

Why is this not a specimen of bronchopneumonia?

This is not a specimen of bronchopneumonia because bronchopneumonia is patchy in distribution and usually does not involve the whole lobe (Fig. 9.3).

What are the histological stages in lobar pneumonia?

1. Stage of congestion
2. Stage of red hepatization
3. Stage of gray hepatization
4. Stage of resolution.

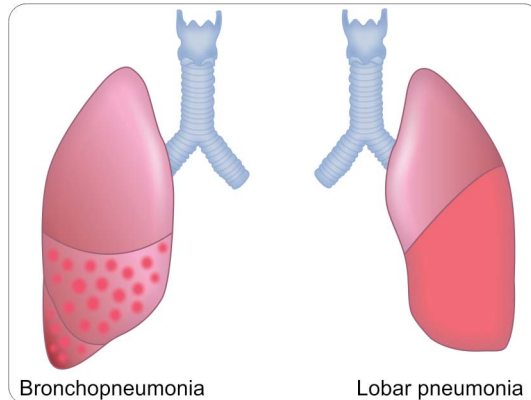


Fig. 9.3: Bronchopneumonia and lobar pneumonia of lung

Describe the stages of lobar pneumonia in short.

| Stages of | Duration | Gross appearance | Microscopic appearance |
|-------------------|---------------------------|---|---|
| Congestion | 1–2 days | Affected lung is: <ul style="list-style-type: none"> • Enlarged • Heavy • Congested • Dark red in color | Typical features of acute inflammation: <ul style="list-style-type: none"> • Dilation and congestion of capillaries • Eosinophilic edema fluid in the air spaces • Numerous bacteria in the alveolar fluid |
| Red hepatization | 2–4 days | Cut surface reveals: <ul style="list-style-type: none"> • Granularity • Red pink in color • Firm with liver-like consistency | <ul style="list-style-type: none"> • The eosinophilic edema fluid is replaced by fibrin strands • Marked neutrophilic exudate with extravasation of RBCs is seen |
| Gray hepatization | 4–8 days | Cut surface reveals: <ul style="list-style-type: none"> • Granularity • Gray in color • Firm with liver-like consistency | <ul style="list-style-type: none"> • Fibrin strands are denser • Neutrophils and RBC reduce in number • Organisms are less numerous |
| Resolution | 8th day to next 1–3 weeks | Affected lobe is gradually restored due to liquefaction of fibrin strands by enzymatic action | <ul style="list-style-type: none"> • Macrophages are the dominant cells • Alveolar capillaries are engorged • Progressive removal of cellular exudate • Restoration of normal lung parenchyma (with aeration) |

What are the complications associated with lobar pneumonia?

1. Empyema
2. Lung abscess
3. Septicemia
4. Delayed resolution
5. Organization and fibrosis.

Miliary tuberculosis of lung**Description**

It is a specimen of a longitudinal section of lung showing numerous uniform small millet size white spots (tubercles) surrounded by areas of intense congestion.

- So, the specimen is identified as “Miliary tuberculosis of lung” (Figs 9.4A and B).

What does the term “Miliary” suggest?

The adjective “miliary” is derived from the similarity of the foci of consolidations to millet seeds.

How does one get Miliary TB of lung?

- Miliary pulmonary disease is sequelae of progressive TB.
- It occurs when organisms (tubercle

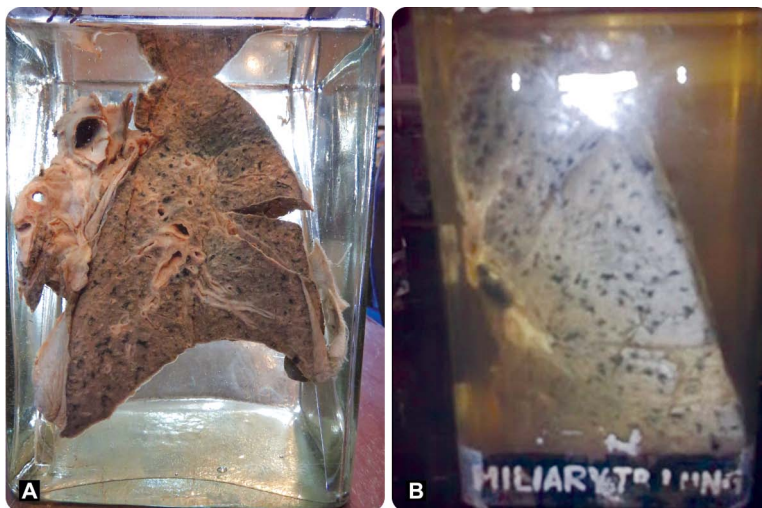
bacilli) draining through lymphatics enter the venous blood and circulate back to the lung.

What are the usual histological findings?

- Individual lesions are either microscopic or small (2 mm) visible foci of yellow-white consolidation scattered throughout the lung parenchyma.
- Miliary lesions may expand and coalesce, resulting in consolidation of large regions or even whole lobes of the lung.

Fibrocaseous tuberculosis of lung**Description**

- It is a specimen of lung showing some thick-walled cavities lined by yellowish-gray caseous material.
- The walls of the cavities are fibrotic and smooth.
- Bronchi and blood vessels are showing thickening.
 - So, the specimen is diagnosed as “Fibrocaseous tuberculosis of lung” (Fig. 9.5).



Figs 9.4A and B: Miliary tuberculosis of lung (Courtesy: Rajkumar Elanjeran, Gandhi Medical College, Hyderabad)



Fig. 9.5: Fibrocaseous tuberculosis of lung

Tuberculosis

What are the forms of tuberculosis in the lung?

- a. Primary TB
- b. Secondary TB
- c. Progressive TB
- d. Miliary TB.

What is Ghon's focus?

- Typically, the inhaled tubercle bacilli implant just above/just below the interlobar fissure (between the upper and lower lobes) and beneath the pleural membrane (so-called subpleural lesion).
- As sensitization develops, a 1–1.5 cm area of gray-white inflammation with consolidation emerges, known as the Ghon's focus.
- In most cases, the center of this focus undergoes caseous necrosis.

What is Ghon's complex?

- In primary TB of lung, tubercle bacilli (in free or phagocytosed form) drain to the regional lymph nodes, which often caseate.

- Ghon's complex is the initial lesion of primary TB. It consists of:
 - A. A subpleural lesion, just above/just below the interlobar fissure (between upper and lower lobes)
 - B. Enlarged caseous peribronchial lymph nodes.

What is the fate of Ghon complex?

- It heals in about 90% of cases by:
 - Fibrosis
 - Calcification
 - Ossification.
- In unfavorable cases (10%), increased hypersensitivity reaction leads to progressive pulmonary TB.

When does secondary TB occur?

- Secondary tuberculosis is the pattern of disease that arises in a previously sensitized host.
- It commonly appears many years after the initial infection, usually when host resistance is weakened.
- It most commonly stems from reactivation of a latent infection.

What is Assman's focus?

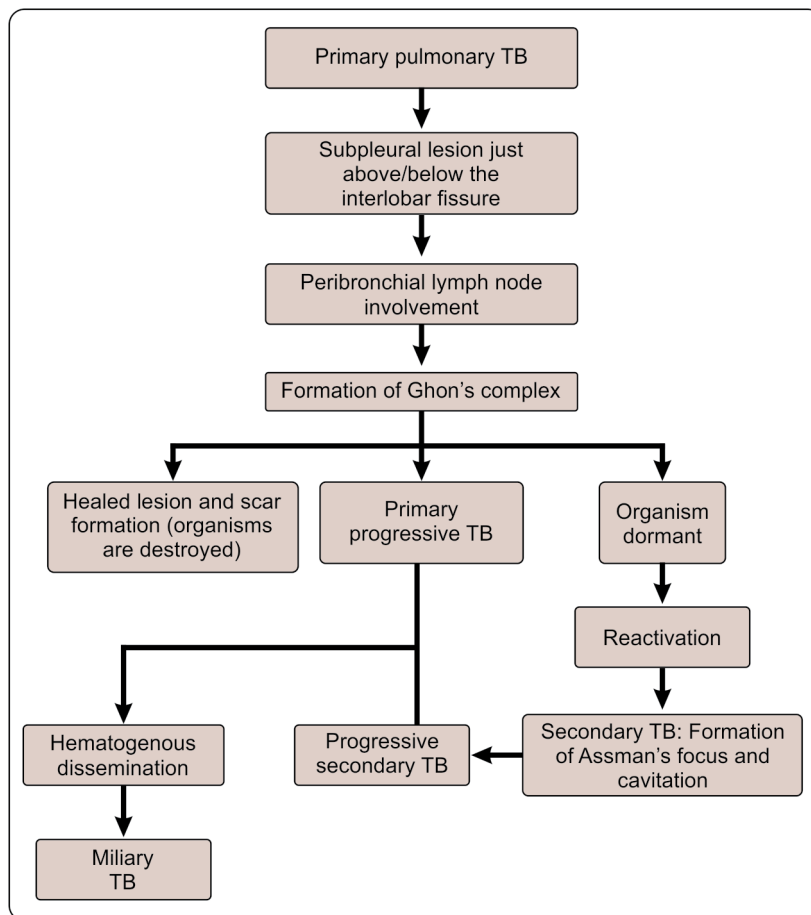
- In secondary TB, the initial lesion is seen characteristically at the apex of the upper lobe of a lung (so-called apical lesion).
- Usually there is only little lymph node involvement (usually infraclavicular lymph node).
- This initial apical lesion in secondary TB (consisting of apical lesion and infraclavicular lymph node involvement) is called Assman's focus.
- Histologically, similar to Ghon focus, it has a central caseous necrosis which is surrounded by a granulomatous inflammatory reaction.
- In most cases, destruction of lung tissues leads to cavitation.

Describe the lesions found in progressive pulmonary TB.

- Progressive pulmonary TB may be a

consequence of progression of both primary and secondary TB.

- In a typical case, the initial lesion (subpleural lesion and apical lesion in primary and secondary TB, respectively) enlarges and erodes into the adjacent lung tissue and finally, into a bronchus.
- Through the eroded bronchus, the partially liquefied caseous necrotic tissue is drained, leaving a ragged, irregular cavity; the walls of the cavity become fibrotic.
- Growth and multiplication of tubercle bacilli are extensively enhanced in this condition as a cavity provides increased oxygen tension.
- This stage of the disease is called "Fibrocaceous TB of lung".
- If disease is not treated at this point, it may progress to involve the entire lobe with marked tissue destruction and fibrosis; resulting in "Tuberculous bronchopneumonia".
- When organisms draining through the lymphatics enter venous blood and circulate back to the lung, it results in "Miliary tuberculosis", small foci of consolidation spread throughout the lung, resulting in large areas of consolidation when they coalesce.



What is isolated tuberculosis?

- It may appear in any of the organs or tissues where the tubercle bacilli lodge hematogenously.
- Organs that are commonly involved include:
 1. The meninges (tuberculous meningitis)
 2. Kidneys (renal tuberculosis)
 3. Adrenals (formerly an important cause of Addison disease)
 4. Bones (osteomyelitis)
 5. Fallopian tubes (salpingitis)
 6. Vertebrae (Pott disease).

What is the most common presenting feature of extrapulmonary TB?

- Lymphadenitis is the most frequent presentation of extrapulmonary tuberculosis, usually occurring in the cervical region (scrofula).
- In HIV-negative individuals, lymphadenitis tends to be unifocal and localized.
- HIV-positive people almost always have multifocal disease and systemic symptoms.

What is nonreactive TB?

- In cases of very low host resistance (as in old age, AIDS, leukemia, persons receiving immunosuppressive drugs, etc.), the lesions show no cellular response.
- The lesions contain high amount of tubercle bacilli and are highly infective.

What is the confirmatory diagnosis of tuberculosis?

- Culture is the gold standard because it also allows testing of drug susceptibility.

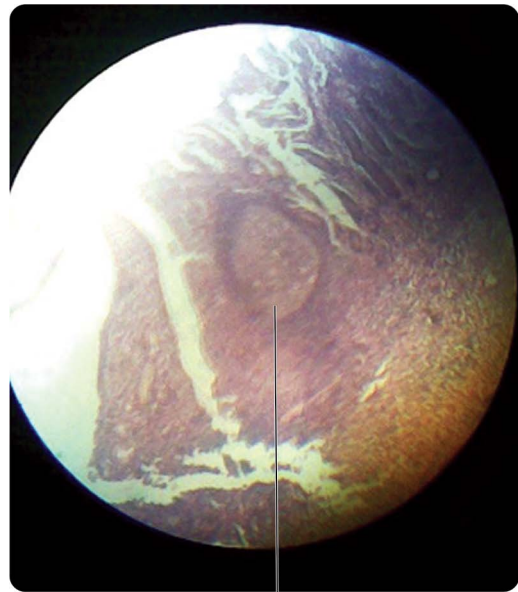
- Conventional cultures require up to 10 weeks, but culture in liquid media can provide the result within 2 weeks.

What is the hallmark of activity and immunity in chronic TB infection?

Caseation and fibrosis, respectively.

Describe the histology of a tubercle.

- Section showing histology of lymph node.
- There is an area of granuloma containing: (Fig. 9.6)
 - Central necrosis with amorphous granular debris surrounded by focus of activated macrophages (epithelioid cells), rimmed by fibroblasts, lymphocytes, histiocytes, occasional Langhans giant cells.
 - It also may contain variable numbers of acid-fast bacilli.



Granuloma formation

Fig. 9.6: Slide showing granuloma in a case of intestinal TB

Bronchogenic carcinoma

Description

- It is a specimen of lung exposing main and major bronchi.
- There is a yellowish-white and darkish growth arising from major bronchus, spreading both within and outside the bronchus and in the wall.
 - So, the specimen is identified as “Bronchogenic carcinoma” (Figs 9.7A and B).

What are the predisposing factors to CA lung?

1. Cigaret smoking: Most important single risk factor.
2. Industrial hazards:
 - High dose ionizing radiation
 - Asbestos
 - Uranium
 - Nickel
 - Chromium.
3. Air pollution:
 - Radon.
4. Genetic susceptibility: Mutations in the following genes are commonly associated with lung cancer:
 - c-MYC
 - KRAS
 - EGFR
 - c-MET

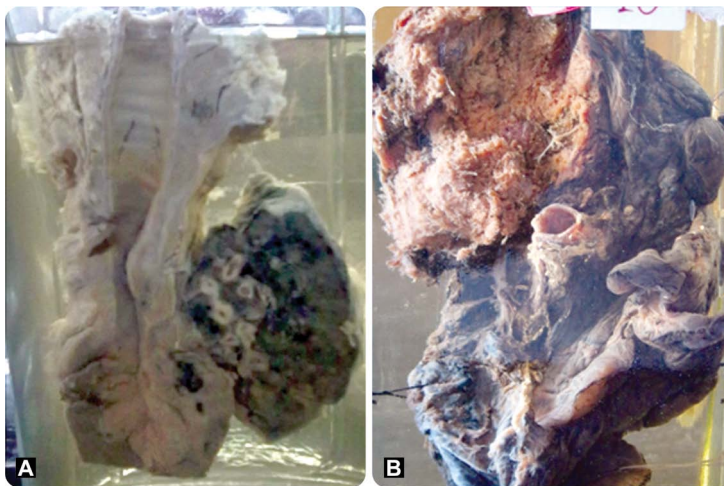
- c-KIT
- CYP1A1.

Describe the histologic classification of bronchogenic carcinoma.

1. Squamous cell carcinoma
2. Small-cell carcinoma
3. Adenocarcinoma:
 - a. Acinar
 - b. Papillary
 - c. Bronchioloalveolar
 - d. Solid
 - e. Mixed subtypes.
4. Large-cell carcinoma.
5. Adenosquamous carcinoma.
6. Carcinoid tumor:
 - a. Typical
 - b. Atypical
7. Carcinomas of salivary gland type.

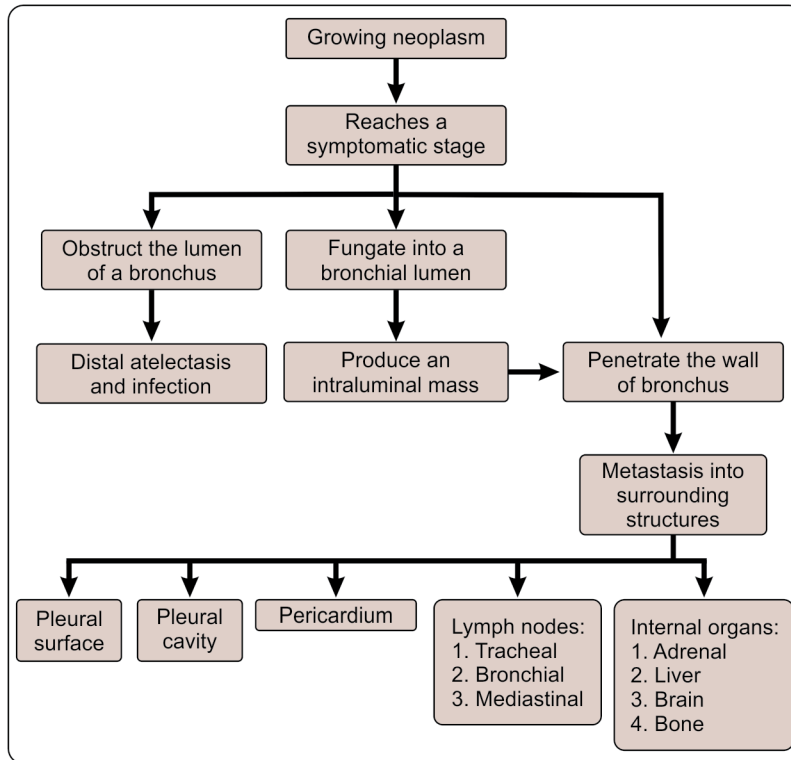
From which area does lung carcinoma originate?

- Lung carcinomas arise most often in and about the *hilus of the lung*.
- About 75% of the lesions take their origin from first-order, second-order, and third-order bronchi.
- Some of the primary carcinomas of the lung arise in the periphery of the lung from the alveolar septal cells or terminal bronchioles.



Figs 9.7A and B: Bronchogenic carcinoma

Describe how lung carcinoma destroys lung tissue and additional structures.



Describe the path of metastasis of lung carcinoma.

- Distant spread of lung carcinoma occurs through both lymphatic and hematogenous pathways.
- These tumors often spread early throughout the body except for squamous cell carcinoma, which metastasizes outside the thorax late.
- The **adrenals** are most commonly involved in >50% of cases.
- The liver, brain and bone are also favorable sites of metastases.

What is the specialty of growth pattern of bronchioloalveolar carcinoma?

- This type of carcinoma arises in the terminal bronchioloalveolar regions.
- Histologically, the tumor is charac-

terized by a pure bronchioloalveolar growth pattern with no stromal/vascular/pleural invasion.

- They grow along the pre-existing structures without destruction of surrounding alveolar architecture.
 - So, this type of growth pattern has been termed “**lepidic**” growth.

What is the histologic specialty of squamous cell carcinoma?

- Histologically, this tumor is characterized by presence of:
 - Keratinization and/or
 - Intercellular bridges.
- Keratinization occurs in the form of:
 - Squamous pearls (Fig. 9.8)
 - Individual cells with dense eosinophilic cytoplasm.

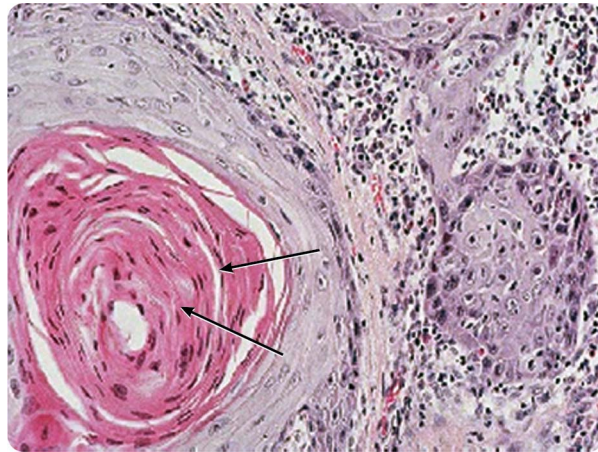


Fig. 9.8: Histological tissue section from a sample of squamous cell carcinoma of lung showing keratin pearls (arrows) formed by layers of keratinization. Reproduced under the permission of National Cancer Institute at National Institute of Health

What is Azzopardi effect?

- It is seen in high grade small cell carcinoma of lung, where necrosis is very common.
- When blood vessels near the tumor is stained with H and E stain, the full thickness of the blood vessel exhibit deeply basophilic staining.
- This occurs due to deposition of DNA and other necrotic materials within the vessel wall.

Which type of lung carcinoma shows highest frequency of p53 mutations?

Squamous cell carcinoma.

Which type of lung carcinoma shows highest frequency of KRAS mutations?

Adenocarcinoma.

What are the anatomic complications caused by lung carcinoma?

1. Emphysema due to partial obstruction of airways.
2. Atelectasis due to total obstruction of airways.

3. Suppurative/ulcerative bronchitis.
4. Bronchiectasis.
5. Lung abscess.
6. Superior vena cava syndrome due to compression of SVC.
7. Pericarditis.
8. Pleuritis.
9. Rib destruction due to chest wall invasion.
10. Horner syndrome due to sympathetic ganglia invasion.

Which histologic variants of lung carcinoma are more associated with paraneoplastic syndromes?

- Small cell carcinomas: ACTH and ADH production.
- Squamous cell carcinomas: Hypercalcemia.

What are the paraneoplastic syndromes caused by lung carcinoma?

The paraneoplastic syndromes caused by lung carcinoma are mainly due to elaboration of various hormones by the carcinoma cells. They are:

| Hormones | Paraneoplastic syndromes |
|--------------------------|--------------------------|
| ADH | Hyponatremia |
| ACTH | Cushing's syndrome |
| PTH | Hypercalcemia |
| Calcitonin | Hypocalcemia |
| Gonadotropins | Gynecomastia |
| Serotonin and bradykinin | Carcinoid syndrome |

Bronchiectasis

Description

It is a specimen of cut section of lung with marked dilation of the bronchi and bronchioles with fibrosis in the adjoining areas.

- So, this specimen is identified as “Bronchiectasis” (Fig. 9.9).



Fig. 9.9: Bronchiectasis. This slice of lung shows extensive, peripheral honeycombing (architectural distortion) in upper and lower lobes. The cystic spaces represent bronchiolectasis. The dark brown areas in the upper lung represent normal lung parenchyma. Reproduced under the permission of Martha L. Warnock, University of California, San Francisco

Define bronchiectasis.

Bronchiectasis is a disease characterized by permanent dilation of bronchi and bronchioles caused by destruction of the muscle and elastic tissue, resulting from a chronic necrotizing infection.

What are the two major pathological points associated with bronchiectasis?

Obstruction and infection.

What are the types of bronchiectasis and what are their causes?

| Types | Causes |
|------------------------|---|
| Obstructive | It occurs by partial/complete obstruction of bronchial lumen by any of the following causative agents: <ul style="list-style-type: none"> • Neoplasm • Foreign body • Mucus secretion • Lymphadenopathy |
| Infective/Inflammatory | It occurs due to repeated episodes of infections. Most common causes are: <ul style="list-style-type: none"> • Pneumonia • Pertussis Some of the rare causes are: <ul style="list-style-type: none"> • Kartagener's syndrome • Primary ciliary dyskinesia (These 2 diseases are associated with abnormality in ciliary movements and subsequent accumulation of bacteria) |

What are the important features of bronchiectasis?

- They usually affect the lower lobes of the lungs bilaterally.
- The bronchi and bronchioles are extensively dilated.
- The walls of bronchi and bronchioles are intensely inflamed.

- There are areas of desquamation and ulceration of epithelial lining.

What are the complications of bronchiectasis?

1. Hemoptysis
2. Lung abscess
3. Fibrosis
4. Amyloidosis
5. Bronchopleural fistula
6. Squamous metaplasia and squamous cell carcinoma (due to extensive desquamation of the epithelial lining, susceptibility to metaplastic changes increases greatly).

SECTION-II

SLIDES

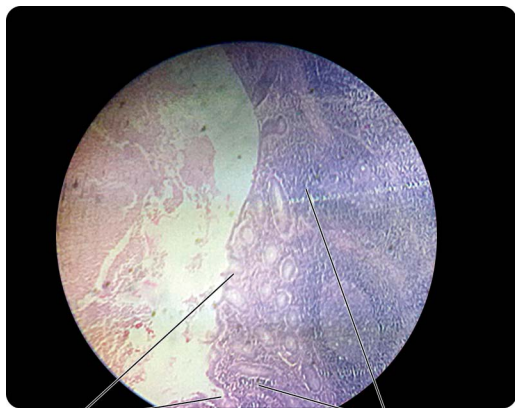
Pathology Practical Slides Identification

CHAPTER

10

Acute appendicitis

- A. Section showing histology of appendix.
- B. Lumen is filled up with acute inflammatory infiltrate of neutrophils, macrophages, fibrin, RBC, degenerated epithelial cells, etc.
- C. Mucosa—Necrosed and ulcerated.
- D. Submucosa and muscle layer—Intense infiltrate of neutrophils and eosinophils (Fig. 10.1).



Ulceration of mucosa Dense inflammatory infiltrate in submucosa and muscle layer

Fig. 10.1: Acute appendicitis

Chronic cholecystitis

- A. Section showing histology of gallbladder (absence of submucosa).
- B. Mucosa—Ulcerated (Fig. 10.2).



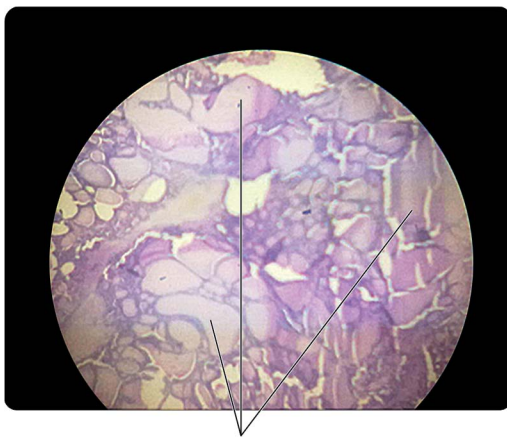
Ulceration of mucosa RA sinus Dense inflammatory infiltrate

Fig. 10.2: Chronic cholecystitis

- C. Dense infiltration of macrophages, lymphocytes and plasma cells.
- D. There is presence of RA sinus (Rokitansky-Aschoff sinus) which is formed by invagination of the discontinuous mucous membrane into the muscle layer and forming gland-like structure.

Colloid goiter

- A. Section showing histology of thyroid tissue.
- B. Glands are dilated and filled up with deeply eosinophilic colloid.
- C. Lining epithelial cells are low cuboidal or flattened (Fig. 10.3).

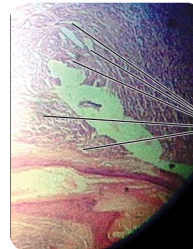
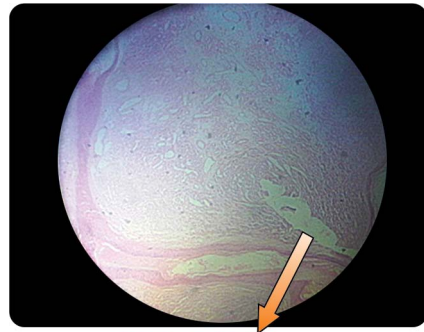


Almost all the follicles contain rich colloid

Fig. 10.3: Colloid goiter

Capillary hemangioma

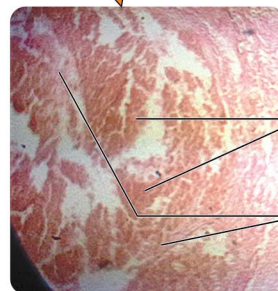
- A. Section showing histology of skin.
- B. In the deep dermis and subcutaneous layer, there are closely packed blood filled capillaries lined by flattened epithelial cells and separated by scant connective tissue stroma (Fig. 10.4).



Closely packed capillaries lined by flattened epithelium

Fig. 10.4: Capillary hemangioma

Cavernous hemangioma



Large vascular spaces
Pale fibrous tissue

Fig. 10.5: Cavernous hemangioma

- A. Section showing a number of large dilated blood filled vascular spaces lined by flattened epithelium (Fig. 10.5).
- B. The vascular spaces are separated by modest connective tissue stroma. Intravascular thrombosis is common.

Tuberculosis of lymph node

- A. Section showing histology of lymph node.
- B. There are areas of granuloma consisting of a granular necrosed material (caseation), surrounded by a zone of epithelioid cells (pale elongated nuclei and abundant pale foamy cytoplasm) along with a few Langhans' giant cells, surrounded by a zone of lymphocytes and that is surrounded by a zone of fibrosis (Fig. 10.6).

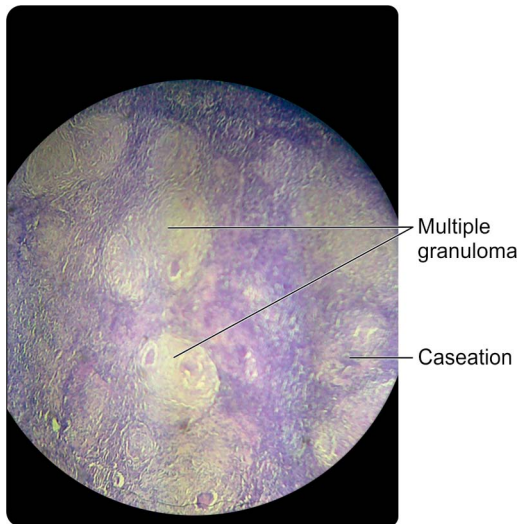


Fig. 10.6: Lymph node TB

Tuberculosis of intestine

- A. Section showing histology of intestine.
- B. There are areas of granuloma

consisting of a granular necrosed material (caseation), surrounded by a zone of epithelioid cells (pale elongated nuclei and abundant pale foamy cytoplasm) along with a few Langhans' giant cells, surrounded by a zone of lymphocytes and that is surrounded by a zone of fibrosis (Fig. 10.7).

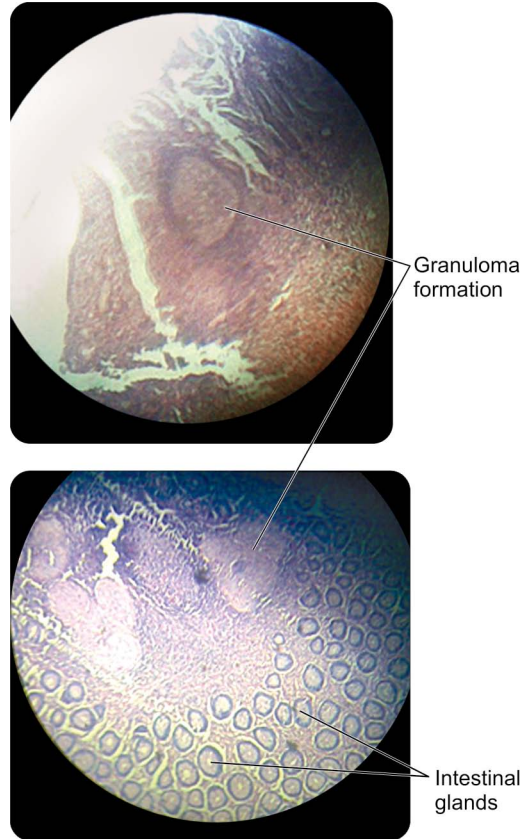


Fig. 10.7: Intestine TB

Adenocarcinoma

- A. Section is showing glandular morphology.
- B. The submucosa and muscle layers are infiltrated by neoplastic cells having large hyperchromatic nuclei, which are arranged in an acinar pattern (Fig. 10.8).

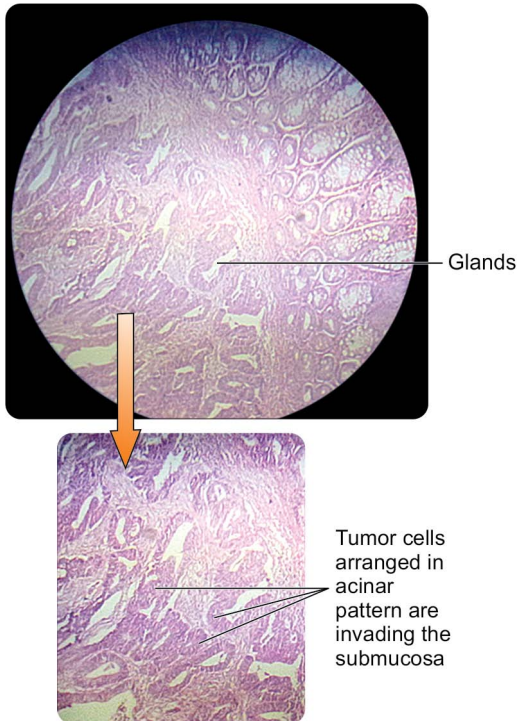


Fig. 10.8: Adenocarcinoma

Secretory endometrium

- Section showing histology of endometrium.
- Endometrial glands are tortuous with

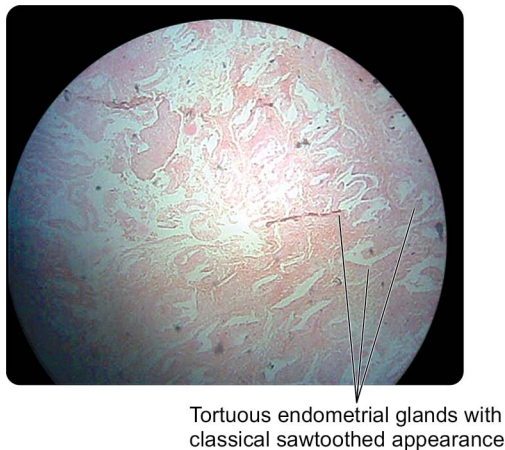


Fig. 10.9: Secretory endometrium

- characteristic *sawtooth appearance* lined by columnar epithelial cells.
- Lumen of glands containing secretion (Fig. 10.9).

Proliferative endometrium

- Section showing histology of endometrium.
- The endometrial glands are more or less uniformly tubular and lined by cuboidal/columnar epithelium.
- Stroma is compact and cellular (Fig. 10.10).

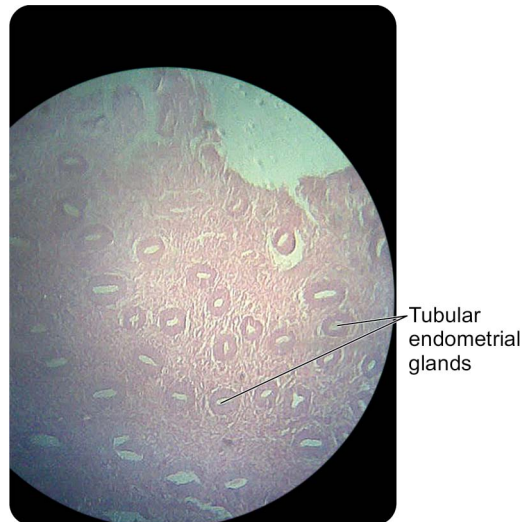
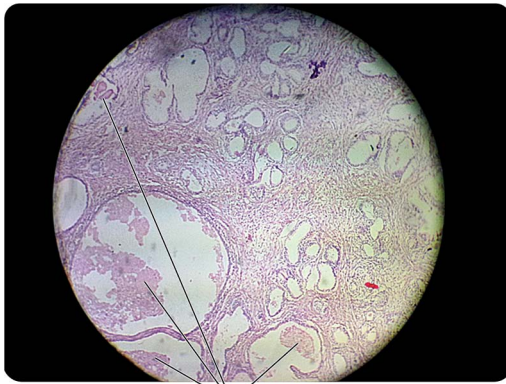


Fig. 10.10: Proliferative endometrium

Benign hypertrophy of prostate (BHP)

- Section showing histology of prostate (fibromusculoglandular nature).
- The glands are lined by columnar epithelial cells with uniform basal nuclei and fine granular pale eosinophilic cytoplasm.
- The gland acini show papillary infolding within the lumen and reddish secretion of the gland, which is called "*Corpora amylacea*" (Fig. 10.11).

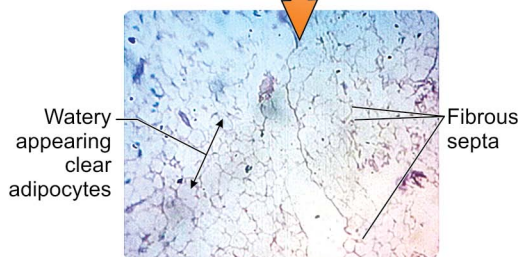
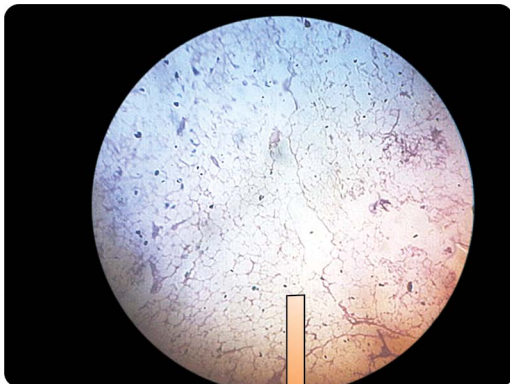


Corpora amylacea

Fig. 10.11: Benign hypertrophy of prostate

Lipoma

- Section showing histology of a tumor composed of normal looking adipose tissue.
- The mass of adipose tissue is separated by irregular fibrous septa (Fig. 10.12).

**Fig. 10.12:** Lipoma

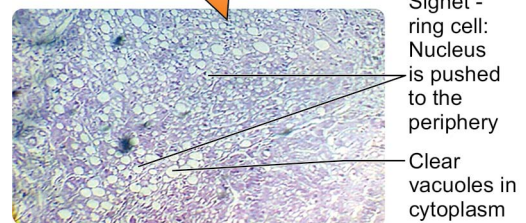
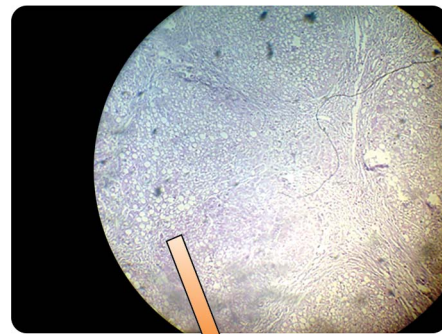
Cirrhosis of liver

- Section showing histology of liver.
- Normal architecture is lost.
- Fibrous band extending from portal tract to central vein and portal tract to portal tract is found.
- Regenerated nodules (micronodule and macronodules) are found (Fig. 10.13).

**Fig. 10.13:** Cirrhosis of liver

Fatty liver

- Section showing histology of liver.
- Normal architecture of liver is preserved.

**Fig. 10.14:** Fatty liver

- C. Hepatocytes show large clear vacuoles in cytoplasm.
- D. Nucleus has been pushed to the periphery by the cytoplasmic vacuoles; the shape is called “Signet-ring” (Fig. 10.14).

Mucinous cystadenoma of ovary

- A. Section showing histology of ovary.
- B. There are multiple cystic spaces lined by single layer of columnar epithelium.
- C. The cystic spaces are separated by fibrovascular stroma and the epithelial cells have uniform basal nuclei and abundant clear cytoplasm (Fig. 10.15).

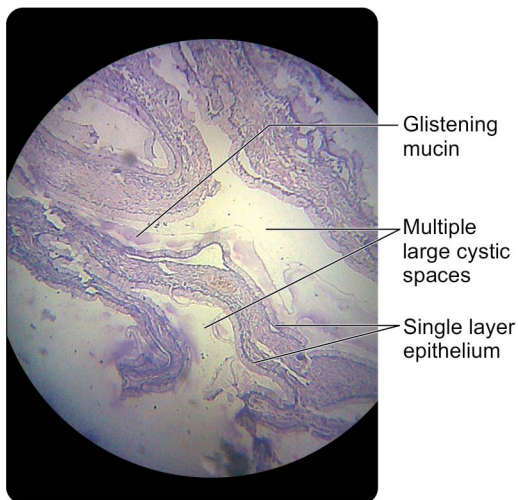


Fig. 10.15: Cystadenoma of ovary

Basal cell carcinoma of skin

- A. Section showing histology of skin.
- B. The dermis is infiltrated by groups of small basophilic round/fusiform cells having prominent dark-stained nuclei

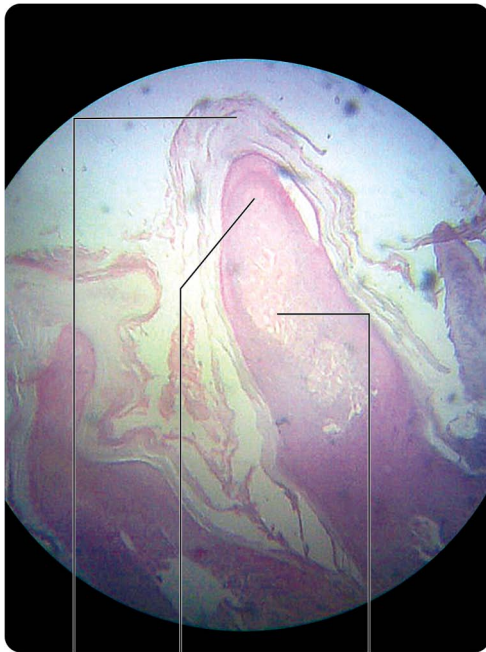
and scanty basophilic cytoplasm, embedded in a mucinous matrix (Fig. 10.16).



Fig. 10.16: Basal cell carcinoma of skin

Squamous papilloma of skin

- A. Section showing histology of skin.
- B. Ridges are elongated and bent inward at both the margins of the lesion.
- C. There are exophytic papillary projections clothed by thickened epidermis.
- D. The papillary processes have a fibrovascular core (Fig. 10.17).



Thickened epidermis Papillary process Fibrovascular core

Fig. 10.17: Squamous papilloma of skin

Squamous cell carcinoma of skin

- Section showing histology of skin.
- The dermis is invaded by atypical squamous cells having hyperchromatic nuclei.
- The neoplastic cells show abnormal keratinization in the form of cell nests deep within dermis (Fig. 10.18).



Abnormal keratinization in the form of cell nests

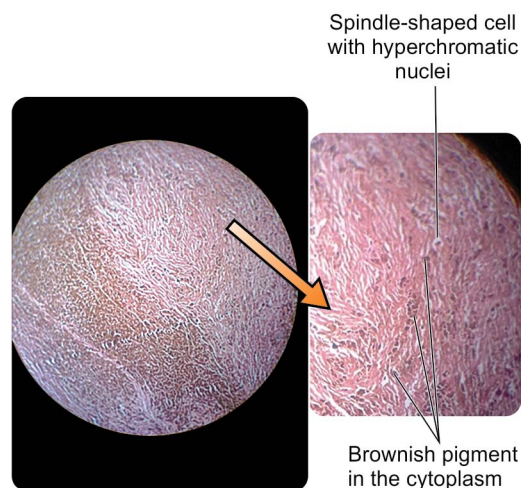


Atypical cells invading the dermis

Fig. 10.18: Squamous cell carcinoma of skin

Malignant melanoma of skin

- Section showing histology of skin.
- There are clumps of spindle shaped-polyhedral cells with hyperchromatic nuclei.
- Some of these cells (melanoma cells) contain brownish pigments in the cytoplasm (Fig. 10.19).



Spindle-shaped cell with hyperchromatic nuclei

Brownish pigment in the cytoplasm

Fig. 10.19: Malignant melanoma of skin

Scirrhou carcinoma of breast

- Section showing islets of cells having hyperchromatic nuclei and scanty cytoplasm.
- The groups of neoplastic cells are surrounded by abundant dense fibrous tissue (Fig. 10.20).

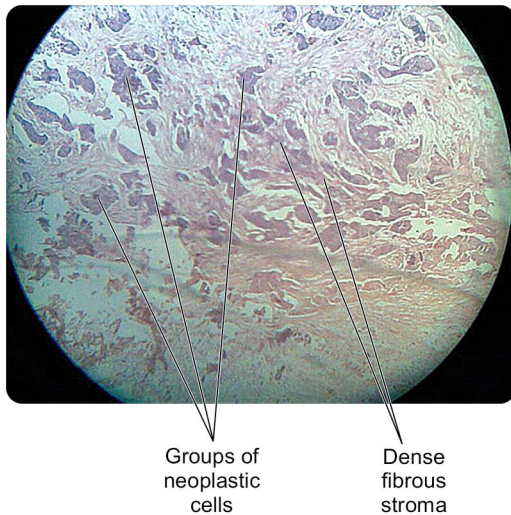


Fig. 10.20: Scirrhou carcinoma of breast

Fibroadenoma of breast

- Section showing elongated branching compressed mammary ductules.
- In between the ductules there are abundant pale fibrous tissue/stroma pressing the ductules (Fig. 10.21).

- clear cytoplasm. (possibly clear cell carcinoma)
- The cells are arranged in sheets and cords with scanty fibrovascular stroma (Fig. 10.22).

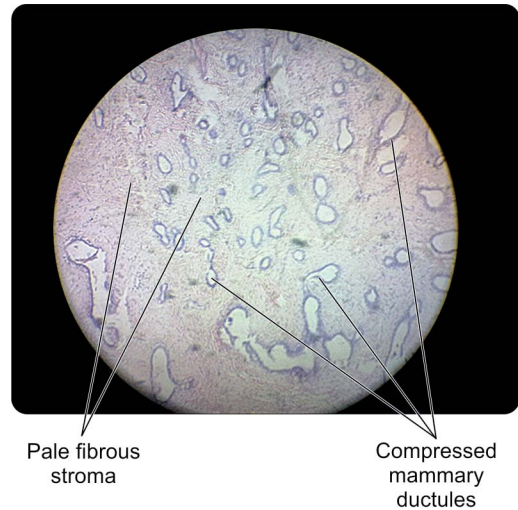


Fig. 10.21: Fibroadenoma of breast

Renal cell carcinoma

- Section showing histology of kidney.
- Elsewhere the section shows tumor cells with dark pyknotic nuclei and

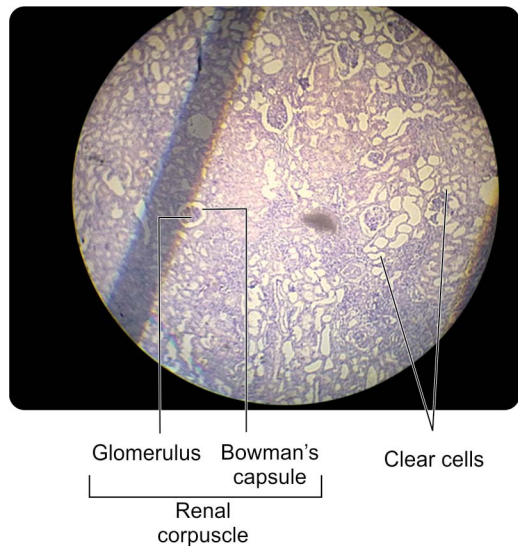


Fig. 10.22: Renal cell carcinoma

Pleomorphic salivary adenoma

- Section showing histology of a tumor composed of many small glands lined by cuboidal epithelium.
- The lumen contains eosinophilic secretion.
- There is abundant myxochondroid stroma (Fig. 10.23).

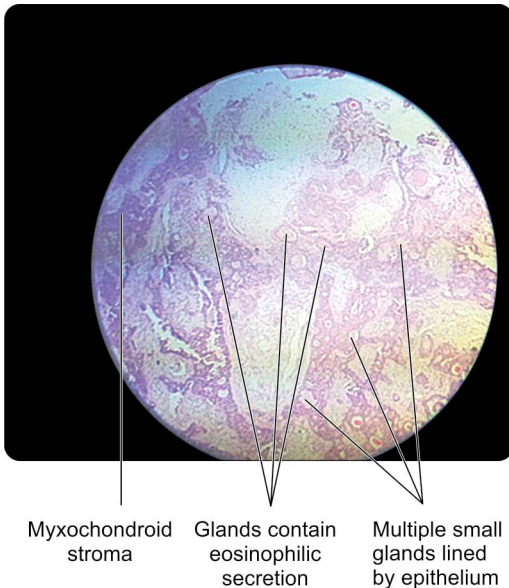


Fig. 10.23: Pleomorphic salivary adenoma

Seminoma testes

- Section showing histology of a tumor composed of sheets of uniform cells divided into poorly demarcated lobules by delicate fibrous septa with lymphocytic infiltrate.
- Seminoma cells are large and round, having a large central nucleus and a clear watery cytoplasm.
- The cytoplasm contains variable amount of glycogen which is washed during slide preparation (Fig. 10.24).

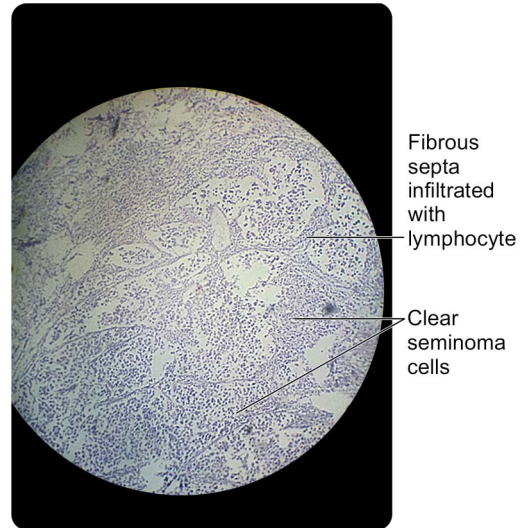


Fig. 10.24: Seminoma testes

Giant cell tumor of bone

- Section showing histology of tumor containing many osteoclastic giant cells in a background of mononuclear stromal cells.
- The cells have large number of vesicular nuclei and moderate amount of cytoplasm.
- There may be areas of hemorrhage and necrosis (Fig. 10.25).

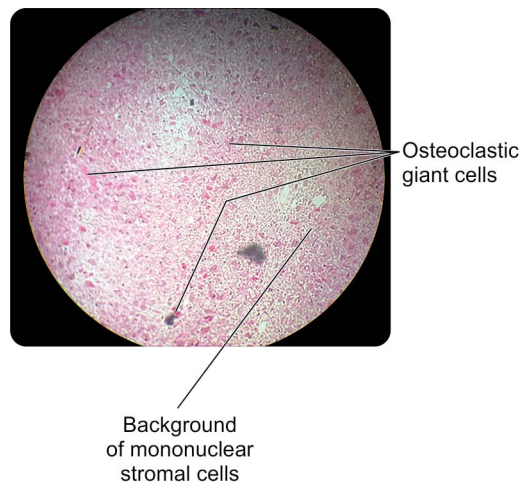


Fig. 10.25: Giant cell tumor of bone

Osteosarcoma

- A. Section showing histology of a tumor composed of dark-stained elongated oval pleomorphic cells.
- B. They form the dense lace-like pattern of neoplastic bone formation (Fig. 10.26).

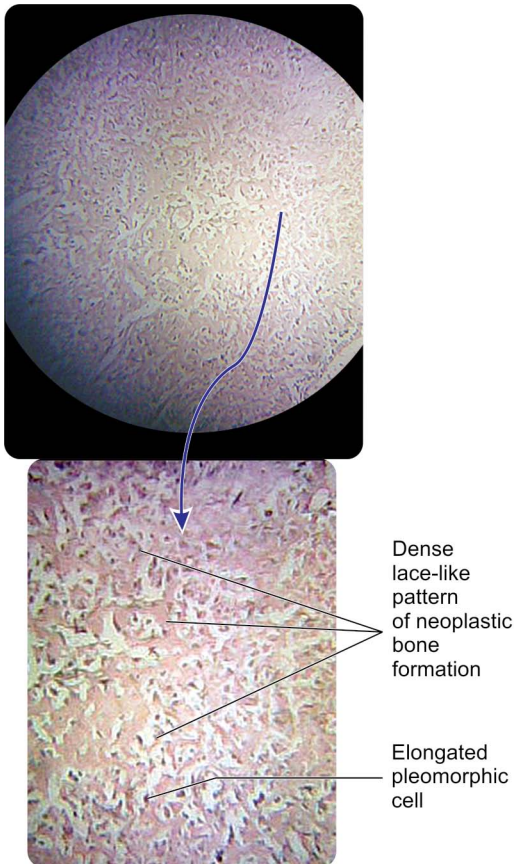
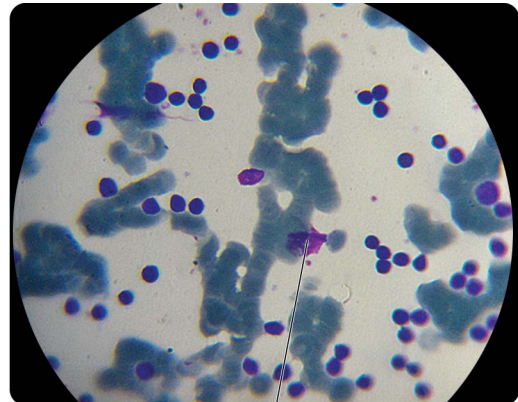


Fig. 10.26: Osteosarcoma

Chronic lymphocytic leukemia (CLL)

- This peripheral blood smear is showing numerous small lymphocytes with condensed chromatin and scant cytoplasm.

- A disrupted tumor cells (smudge cell) is being seen in the center, which is characteristic of CLL.
- Spherocytes (hyperchromatic, round erythrocytes) can also be seen (Fig. 10.27).



Smudge cell is characteristic of CLL

Fig. 10.27: Chronic lymphocytic leukemia

Chronic myeloid leukemia (CML)

- Peripheral blood smear is showing numerous mature neutrophils and some metamyelocytes (Fig. 10.28).

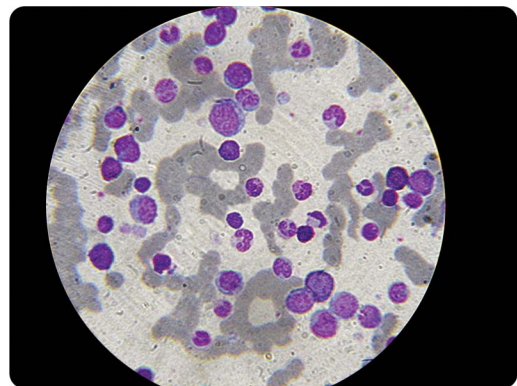


Fig. 10.28: Chronic myeloid leukemia

Bibliography

1. Bailey, Love. A Short Textbook of Surgery, 25th ed.
2. Brunickardi CS. Schwartz's Principles of Surgery, 9th ed.
3. Essential Orthopaedics, 4th ed. Maheshwari.
4. Faust T, Reddy KR. The Clinician's Guide to Liver Disease.
5. Guidelines on Renal Cell Carcinoma by European Association of Urology, April 2010.
6. Huckstep RL. Typhoid fever and other salmonella infections. Edinburgh, E and S. Livingstone Ltd, 1962.
7. Kleiner DE, Brunt EM, Van Natta M, Behling C, Contos MJ, Cummings OW, Ferrell LD, Liu YC, Torbenson MS, Unalp-Arida A, Yeh M, McCullough AJ, Sanyal AJ. Nonalcoholic Steatohepatitis Clinical Research Network. Design and validation of a histological scoring system for nonalcoholic fatty liver disease. Hepatology. 2005 June;41(6):1313–21.
8. Park's Textbook of Community Medicine, 22nd ed.
9. Rheumatic fever and Rheumatic heart disease: Report of a WHO expert consultation: 29th October- 1st November, 2001.
10. Robbins, Cotran: Pathologic Basis of Disease, 8th ed.

Index

Page numbers followed by *f* refer to figure and *t* refer to table

A

Adenocarcinoma 94, 103, 104*f*
Adenovirus 88
Alcoholic fatty liver disease, pathogenesis of 36
Amyloid kidney 49
Amyloidosis 98
Aneurysmal bone cyst 84
Anitschkow cells 7*f*
Anorexia 28
Aorta, abdominal 12
Aortic and mitral valvular diseases 15
Appendicitis 101, 101*f*
Arteries 12
Aschoff bodies 6, 6*f*
Assman's focus 91
Atheroma 11, 11*f*
 evolution of 12
Atherosclerosis, pathogenesis of 12*f*, 13*f*
Atherosclerotic plaque 12

B

Bacterial endocarditis, acute 11
Basal cell carcinoma of skin 106, 106*f*
BHP
 pathogenesis of 65, 66*f*
 sequelae of 67
Bleeding 23
Blood vessels 14
Bone
 giant cell tumor of 82, 82*f*, 84, 109, 109*f*
 osteoblastic tumors of 86
Brain 13
Breast 74
 cancer 77*f*
 carcinoma 74, 74*f*, 75, 76
 fibroadenoma of 108, 108*f*
 scirrhous carcinoma of 108, 108*f*
Brinton's disease 25
Bronchiectasis 96, 97, 97*f*
 complications of 98
 types of 97
Bronchitis 31

Bronchogenic carcinoma, classification of 94
Bronchopneumonia 31, 89, 89*f*

C

Cancer
 cervix, progression of 70
 ulcer 26
Carcinoma
 adenosquamous 94
 breast 74, 75*f*
 bronchioloalveolar 95
 bronchogenic 94, 94*f*
 cervical 69
 cervix 69, 72
 types of 69
 colon 31, 33
 of colon 31*f*
 penis 63, 63*f*
 types of 63
Caterpillar cells 7*f*
Cervical carcinoma, pathogenesis of 69
Cholecystitis 31, 101, 101*f*
Chondroblastoma, benign 74
Chondromyxoid fibroma 84
Chronic GN, treatment of 54
Cirrhosis 47
 alcoholic 22
 mention complications of 46
 of liver 40, 40*f*, 41, 105, 105*f*
 WHO definition of 41
Codman's triangle 86, 86*f*
Colloid goiter 102, 102*f*
Colon cancer, types of 33
Comedocarcinoma 76
Community-acquired
 acute pneumonia 88
 atypical pneumonia 88
Congestion 31
 stage of 89
Congestive cardiac failure 9, 16
Coronary arteries 12
Corpora amylacea 104

Coxiella burnetii 88

Cyst, torsion of 73

Cystic teratoma

benign 72, 72f, 73

complications of benign 73

D

Dermoid cyst 72, 72f, 73

Diabetes mellitus 12

Diabetic nephropathy 52

Diarrhea 28

Diffuse stomach cancer 25

Distal radius, GCT of 84f

Dysphagia 9

degree of 71

Dysplastic cervical epithelium 71

E

Empyema 90

Endocarditis 7

Escherichia coli 79, 88

Esophagus, lower part of 21

F

Fatty liver 35, 35f, 36f, 39, 40f, 105, 105f
disease, alcoholic 42

Fatty streaks 12

Fever 28

Fibrillation, atrial 9

Fibrinous pericarditis 17, 17f, 18

Fibrocaceous tuberculosis of lung 90, 91f

Fibrosis 98

Fistula, bronchopleural 98

Focal segmental glomerulosclerosis 51

G

Gastric carcinoma 21, 23, 23f, 26

pathogenesis of 24

spread of 26

types of 24, 25f

Gastrointestinal tract 20

Ghon's

complex 91

focus 91

Glomerulonephritis, chronic 53

Glomerulosclerosis 52

Granular contracted kidney 52, 53, 53f

Gray hepatization, stage of 89

Great vessels 13

H

Haemophilus influenzae 79, 88

Hair shafts 73

Heart 13

failure cells 16f

Hemangioma

capillary 102, 102f

cavernous 102, 102f

Hematuria 62

Hemochromatosis, types of 43

Hemoptysis 98

Hemorrhage 47

Hepatic coma 47

Hepatocellular carcinoma 47

Hereditary hemochromatosis 43

Hilus of lung 94

Horner syndrome 96

Hospital-acquired pneumonia 88

Hyalinosis 52

Hydronephrosis 55, 55f, 56

causes of 55

pathogenesis of 56

Hyperchromasia 71

Hyperlipidemia 12

Hyperparathyroidism 22

brown tumor of 84

Hypertension 12, 15

Hypochlorhydria 26

I

Infective endocarditis 10f

Inflammatory carcinoma 76

Intestinal

metaplasia 26

tuberculosis 27

Intestine, tuberculosis of 103

Intraepithelial neoplasia, cervical 71

Ischemic heart disease 15

J

Jejunum 21

K

Kerley B lines 16

Kidney 49

cystic disease of 60

Klebsiella pneumoniae 88

Koilocytic atypia 71

L

- Large
 - cell carcinoma 94
 - intestine 31
 - white kidney 49, 49f
- Late stage chronic glomerulonephritis 54f
- Left ventricular hypertrophy 14f
- Legionella pneumophila* 88
- Leiomyoma 68, 68f
 - malignant counterpart of 69
- Leukopoiesis, suppression of 31
- Linitis plastica 25
 - appearance 26, 25f
- Lipoma 105, 105f
- Liver 34
 - anatomy of 34f
 - metastatic carcinoma of 47, 47f
- Lobar pneumonia 89, 90f
- Lung
 - abscess 90, 96, 98
 - carcinoma 95, 96
 - lobar pneumonia of 87, 88f, 89f
 - miliary tuberculosis of 90, 90f
- Lymph node, tuberculosis of 103, 103f
- Lymphocytic leukemia 110, 110f

M

- Malignant transformation 73
- Meckel's diverticulum 21
- Membranoproliferative glomerulonephritis 49, 52
- Membranous glomerulonephritis 49
- Meningitis 31
- Mitral stenosis 3, 3f
 - complications of 9
 - in RF/RHD, pathogenesis of 4f
- Mitral valve 3, 5, 6, 10f
- Mixed bacterial infections 79
- Moraxella catarrhalis* 88
- Mycoplasma pneumoniae* 88
- Myeloid leukemia, chronic 110, 110f
- Myocarditis 7

N

- Nephrosclerosis, benign 53
- Nephrotic syndrome 51
- Night sweats 28
- Nonalcoholic fatty liver disease 43
 - pathogenesis of 38
- Nucleus, enlarged 71

O

- Obstructive pulmonary disease, chronic 22
- Osteoclastic giant cells 84
- Osteomyelitis 31, 79
 - complications of acute and chronic 80f, 81, 81f
- Osteosarcoma 84, 84f, 85, 85f, 86f, 110, 110f
 - types of 84, 85
- Ovary
 - cystadenoma of 106f
 - mucinous cystadenoma of 106

P

- Pain, epigastric 23
- Painless hematuria, causes of 62f
- Parainfluenza virus 88
- Paraneoplastic syndromes 96
- Peptic ulcer 20, 20, 23,
 - complications of 22
 - pathogenesis of 21
- Pericarditis 7, 18f, 96
 - acute 18
 - chronic 19
 - classification of 18f
- Pleomorphic salivary adenoma 109, 109f
- Pleuritis 96
- Pneumonia, types of 88
- Polycystic kidney 55
 - disease 57, 58f
 - pathogenesis of 58
- Portal cirrhosis 46
- Postinfarction syndrome 18
- Poststreptococcal glomerulonephritis 50
- Pott's disease 81
- Proliferative endometrium 104, 104f
- Prostate, benign hypertrophy of 65, 65f, 104, 105f
- Prostatic hyperplasia, benign 65
- Pulmonary
 - edema, acute 47
 - fibrosis 16
- Pyelonephritis 53, 55
- Pyogenic osteomyelitis, pathogenesis of 80

Q

- Q fever 88

R

- Rapidly progressing glomerulonephritis 49
- Recurrent
 - hemoptysis 9
 - pulmonary edema 16

Red hepatization, stage of 89
 Renal cell carcinoma 60, 108, 108f
 major types of 60
 Renal failure, chronic 22
 Resolution, stage of 89
 Respiratory syncytial virus 88
 Rheumatic fever 3, 4, 18
 Rheumatic heart disease 3, 10
 RPGN, types of 50

S

SABE
 complications of 11
 pathogenesis of 10
Salmonella 79
 typhi 29
 SARS virus 88
 Sawtooth appearance 104
 Sclerosis 52
 Sebaceous glands 73
 Secretory endometrium 104, 104f
 Seminoma testes 64, 64f, 109, 109f
 Septicemia 90
 Sequestrum 78f
 Sickle cell disease 79
 Signet-ring 106
 appearance 39
 Simple bone cyst 84
 Skin
 malignant melanoma of 107, 107f
 squamous
 cell carcinoma of 107, 107f
 papilloma of 106, 107f
 Small cell carcinoma 94
 Spine, tuberculosis of 81, 82f
 Squamous
 cell carcinoma 94, 95, 98
 intraepithelial lesion 71
 metaplasia 98
 Stable plaques 14
Staphylococcus aureus 79, 88

Steatohepatitis, alcoholic 37
 Steatosis 35, 36
 Stenosis 3
 Stomach 20, 21
 Streptococcal cell, structure of 5f
Streptococcus pneumoniae 88
 Subacute bacterial endocarditis 9, 9f
 Superior vena cava syndrome 96

T

TB spine, complications of 81
 Teratoma, types of 73
 Testicular seminoma 64f
 Toxic myocarditis 31
 Tuberculosis 91
 Tuberculous
 osteomyelitis 81
 ulcer 27, 27f
 Tumor, carcinoid 94
 Typhoid
 fever 31
 nodules 31
 rash 31
 ulcer 29, 29f, 30, 31
 complications of 30
 of small intestine 29f
 pathogenesis of 29

U

Ulcerative bronchitis 96
 Ulcers, duodenal 22
 Unstable plaques 14
 Uremia 18
 Uterine leiomyoma, types of 68
 Uterus, leiomyoma of 68, 68f

V

Valvulitis 7
 Viral hepatitis 42
 Viruses 88
 Vomiting 23